

VISION SCIENCE PROBLEMS IN MEDICAL IMAGING: A RESEARCH  
INITIATIVE OF THE NATIONAL CANCER INSTITUTE BASIC BIOBEHAVIORAL  
AND PSYCHOLOGICAL SCIENCES BRANCH

NOVEMBER 6, 2014

00:00:06 TODD HOROWITZ: If I don't know you, she probably suggested that I invite you. So, just a couple notes on logistics first. So, we are being broadcast on a webinar and so again, Amola here is handling that. Some people have requested that their talks not go out, not be broadcast on the webinar because they're presenting unpublished data, which is fine. Most of those people have been moved to the end tomorrow.

00:00:40 So, you might have noticed that we've shuffled the schedule around a little bit. We're trying to optimize the schedule. So, for the most part, people who don't want to be broadcast on the webinar are in the Friday morning session. There are going to be a couple exceptions to that. Lunch, we were trying to arrange Corner Bakery, but they needed like a big order in advance and so we decided it's actually just going to be simpler to eat at the cafeteria here. So, it's a nice big cafeteria, and the food's fine.

00:01:11 And then we'll make an announcement later about where we're going for dinner. We'll make some reservations. And that will be in the Bethesda area near to the hotels. So, a couple notes on the

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meeting format. The aim of the meeting here is to get a lot of discussion going so I've tried to encourage people not to give long talks. And so if you notice on the schedule I have set the talks up in pairs.

00:01:43 So, we're going to have someone talk for ideally five minutes, really no longer than eight with as few slides as you can get away with. And if everything is not clear, if you don't have a chance to present everything, that's fine because then there'll be a lot of time for people to ask questions and to discuss the contents of your talk. And then we'll move on to the second in the pair.

00:02:07 In general I have tried to pair people up so that one of the talks is more from the basic vision science area and one is more from the medical imaging area. That's not true in 100 percent of the cases, but that was sort of my aim. And so then after a couple talks we'll have a longer discussion section. The discussion, we have a series of moderators, people who have graciously volunteered to help keep things going, starting here with Lynne Padgett.

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00:02:39 And then Kristin Litzelman and Becky Ferrer are in the back. Annette Kaufman, are you here? Annette Kaufman will arrive later. And Vinay Pai will do the honors for tomorrow. So, these are my NIH colleagues. And now I thought I'd give you just a quick little introductory talk explaining sort of the philosophy behind the meeting and why I wanted to have it here.

00:03:17 And this is my one slide. Those slides don't count because they were on the logistics. And so the origins of this meeting and my interest in this particular area lie around 10 years ago Jeremy Wilkes [ph.] and I did a series of studies on rare targets in visual search.

00:03:43 And basically what we found was that when targets were rare, it was more difficult to find them. And we were originally doing this in a relatively, you know, with untrained observers in sort of the basic vision science environment. And then it turned out that this phenomenon was already known in the medical

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image perception literature, the prevalence effect  
and had been a topic of some discussion.

00:04:11 And that in turn provided a lot of fertilization for  
the development of our theories about how this worked  
on sort of the basic level and then in turn had  
implications potentially for how we do search through  
complex images like mammograms and so forth. And so  
I had this experience that there is sort of this  
two-way flow between basic science and somewhat more  
applied science where you can get ideas that are  
really interesting in the field in applied areas that  
stimulate ideas about how to do basic research and  
vice versa, that the flow can go both ways.

00:04:48 And I thought that was - that was part of the genesis  
of this meeting. And it's also important to note  
that we didn't just start investigating the rare  
target phenomenon on a whim out of curiosity. This  
was actually inspired by problems brought up in the  
baggage screening process. So, a couple of years  
after the September 11<sup>th</sup> attacks the FAA, which was  
running airport security research at the time,  
decided they needed to get some vision scientists in

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to do research on how to improve the process of  
screening your luggage as you check onto the plane.

00:05:29 And so they got together a meeting, and I can't  
remember, was this VSS or Psychonomics [ph.]? VSS?  
MALE: One or the other.

TODD HOROWITZ: One or the other. But someone from  
the FAA's research lab came and got a whole bunch of  
vision science researchers together and explained  
what the problems are. How do the transportation  
security officers look - how are the images  
constructed?

00:05:59 What are they looking for? What are the various  
problems they encounter? What are the procedures?  
And people started thinking of different aspects of  
that problem that they could do research on. And  
there have been many, many lines of really  
interesting scientific research that came out of that  
that I think are informing the way we do baggage  
screening and have also informed the basic vision  
science.

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00:06:24 And so my idea is to try and replicate that fertilization and get people talking to figure out what are the big problems, what are maybe concepts from vision science that might be applicable, and sort of what really interesting ideas can go the other way. And so that is why that was the origins of this meeting. That has been my dream for the last two years. So, thank you all for coming here and fulfilling my dream. And I hope you will find it as fascinating as I do. And with that, Ragini, let's get started.

00:07:52 RAGINI VERMA: I'm going to talk about connectomics with something called diffusion imaging. So, on my last night's chat with Todd I realized that not many people know much about diffusion imaging. So, and I changed the topic a little bit. I initially said it was connectomics for neuro-oncology, but then we talked a little bit and I said there's connectomics for neuro-oncology and there's connectomics for everything else.

00:08:17 And the reason I'm going to say this is because [unintelligible] in the brain with a brain tumor.

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You really don't need much image analysis. The kind of connectomics that you need for this is very different from the kind of connectomics that you need for a brain like this on the left, which is the brain of a schizophrenia patient.

00:08:38 And you can bring in a hundred psychiatrists in here and they will not be able to tell you the difference between this brain and the brain of a normal person just by looking at it. For that you need a different kind of population-based analysis versus this one when you need to find out how the tumor is connected to the rest of the brain and where you should give radiation treatment so that it reaches the tumor the fastest.

00:09:02 So, what is diffusion imaging? So, think of the brain as a highway network. Okay. So, these are the roads which connect you from one region of the brain to another region of the brain, and there's traffic moving on the road. So, let's stop it for a bit. [inaudible] stop things if I wanted to. And then when I don't want to stop it, that's...

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00:09:27 So, the roadways take the - it's the structure of the brain, so that's the white matter structure. The traffic is your thoughts or the function on it. And all the region in between is the grey matter. Depending on what you wanted to capture, you pick a different imaging modality. Diffusion imaging gets you the roadways all the time.

00:09:50 If you see those crossings in between, that's very difficult for DTI. You might have heard diffusion tensor imaging. Because of the way you fit the mathematical model it cannot get you a crossing. So, you fit a higher order model and you call it something else fancy as high angular resolution diffusion imaging. All it gets you is the white matter pathways in the brain and tells you the grey matter is mush. You can try and do something with it, but diffusion imaging is not the way to go for that.

00:10:19 That being said, so this is diffusion imaging. What happens inside surgery? So, now we are going to just talk about very quickly the use in surgery and outside of surgery. So, this is what a surgeon sees.



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This is on the left-hand side. This is the brain.  
He's trying to get an entry into the brain. There is  
a tumor right there. And this is up close. So, they  
just have a pointing device which tells them this is  
the quickest path to get to the tumor right there.

00:10:48 And I'm sorry. This might be a little bit queasy for  
just around breakfast, but this is what the brain  
looks like when they open it up. They actually put  
these numbers in there just to find out how they're  
stimming [ph.] and getting to - rather the only thing  
they want to save is eloquent function, vision, motor  
movement, and language, basics, just the basics.

00:11:15 So, they will go and stim. They will find out the  
points right out there, so here, and they'll say  
these are all negative points, and they make their  
first incision there after they remove. It's as  
basic as that. The surgeon keeps everything in his  
head. So, anything you can do to make it safer, it's  
just wonders for the surgeon.

00:11:37 It's like giving you an access and saying I'm going  
to give you an arrow that says there is a car coming

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from behind on the left-hand side. Will you stop using your eyes? No. But that arrow makes it so much safer for you. That's exactly what diffusion imaging does for a surgeon. It just makes it safer.

00:11:55 So, when you do planning, you give them these fiber tracts, which is just a visualization of the white matter pathways in the brain. And this black region here is the tumor, and you draw a circle around it to tell them this is your safety zone. If you go any further, you're going to hit one of those tracts or you're going to hit the [unintelligible] and there's going to be some kind - arcuate gives you language, ILF and IFOF give you more cognitive function. So, basically if you want to decide I don't want you to lose the functionality of tasting my wine, you need to go to IFOF and ILF.

00:12:32 But if you just want basic language, you would go to arcuate. So, this is connectomics when you're a surgeon. Very basic, but this visualization is needed to tell the surgeon how far he can go and how he can proceed as a tunnel through the top of the

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brain into the tumor without hurting much white matter tissue.

00:12:53 The other kind of connectomics that we do now establishes that things get cut, but never mind. Two things, one is the tumor, which tells you gross understanding of these white matter pathways in the brain and how to find that this region is--mush here-- in the brain. It's called edema, which means a lot of water in the brain. So, diffusion imaging is able to tell you how to get through the water depending on the different kinds of diffusion imaging.

00:13:25 But a very important visualization aspect is when you try and combine modalities, which is the function and the diffusion, which is important for the surgeon. The red is the function activation in the brain that tells you - this is an awake surgery, which I showed you, which means the patient is talking back to the surgeon as the surgery is going on.

00:13:47 So, the function will tell you language is still activated as overlay with diffusion and try and get

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you the measure. Ultimately what we have talked about, neuro-oncology and everything else. This is what a connectome as it looks like in the brain. You divide the brain into multiple regions, go set up pathways between one region to another, set up a graph theory model if that is your choice, and then try and do statistics on it.

00:14:19

So, this was a study in which we tried to find differences between men and women. The left-hand side are women, which shows you they connect left to right, men connect front to back, which means perception to action, logic, and infusion [ph.]. Do you need a \$12 million study to show that? Maybe not, but if this was a study going from 6 to 18 years, which tries to see whether there is a progression in differences in psychopathology, and since psychopathology progresses differently in men and women, the idea was to try and study this.

00:14:56

And I leave you with that, which is you can either look at this this way or you can visualize it in terms of subnetworks and try to find coherent

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cognitive deficiencies just based on subnetworks.

And that's about it. Thank you so much. [applause]

00:15:22 [no audio]

00:15:56 LYNNE PADGETT: Turn on the mic, the red light will  
come on for your question [inaudible].

00:16:02 MALE: So, my question was is there any kind of real-  
time imaging available for the surgeon?

00:16:07 RAGINI VERMA: There is internal MRIs, except it's  
used only for very basic [ph.] very few places, very  
expensive. You also need to go very, very, very,  
very quick. So, diffusion imaging kind of fails in  
that. They do require diffusion imaging, but it's  
only to see that you haven't cut the pathway. That's  
about it.

00:16:32 MALE: So, I'm just wondering if there's a - it seems  
like all the roots and everything where it's clearly  
visualized, are there perceptual issues in providing  
this kind of feedback to surgeons? Is there a  
perceptual question on image - on perception, on

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visual perception, is the visualization effective or  
are there still limitations there?

00:16:56 RAGINA VERMA: It is a visualization of an axon. An  
axon is in micrometers. This is actually in  
millimeters. So, there is an issue of saying to the  
surgeon that what you see, he still has to use  
something in his [unintelligible], which is  
[unintelligible] the tissue has become - it's soft  
[ph.] tissue, right. So, this was pre. And this is  
all done pre. This is not being done as the surgeon  
is cutting the brain open.

00:17:25 MALE: So, the surgeon has to predict the deformation  
of the tissue.

RAGINA VERMA: Absolutely. So, brain  
[unintelligible] is huge.

MALE: And they have to use the visualization of the  
tract or whatever the tractography or whatever in  
order to predict where the connection will be. And  
are they going to have to look at that and interpret  
what that image means? Because it may not exactly  
mean what you think. In other words, if you have a  
little tract that goes from here to there, does that

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mean that there are some population of neurons that go from here to there or just on average they go that way?

00:17:59 RAGINA VERMA: There is a population of neurons that go from there to there except it's a computer environment, right. So, it depends on a bunch of parameters and you, I mean we as the imaging scientist have to tell the surgeon that if it is not going somewhere, it does not always mean that there is no tract. It means that your parameters did not detect it. That's why the whole area is about validation.

00:18:25 So, you do a stim and you see okay, you're [algorithm] and the stim gave it so your algorithm is correct. If you have edema, diffusion is all about measuring water. If you have water or swelling in the brain, it will change the diffusion completely. So, it might not work then. So, for the surgeon this is only a planning tool which will tell you that this is how I should proceed and go in. And after that, once he opens the brain - so, this is the brain.

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00:18:52        The moment you open the skull, the brain pushes out like this. All bets are off. At that moment right there all bets are off. If it's not an awake surgery, they give you something to reduce the swelling. So then whatever is in his head is still mostly valid [ph.] inside the brain. But if it's an awake surgery, then they can't give you anti-swelling things because they are paralytics [ph.].

00:19:18        So, the brain does come out. It shifts. Exactly. It shifts the navigation system which tells them what to look for. It doesn't tell you every second whether he should turn left or right. It's just not reached that level yet.

00:19:34        MALE: So, with all of these computer-aided navigation detection things, there are at least two possibilities. One is that they are underused and that the physician declines to use a perfectly lovely signal that you are providing. And the other is that they overuse it and trust the, in your case the connections that you're putting up, more than they should.



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- 00:20:04 Is there any data on the degree to which either of these things are happening and the degree to which this sort of information that you're providing actually improves outcome?
- 00:20:17 RAGINA VERMA: Yes. There have been several studies that show that if you do a neuro-navigation system, it has improved. There are also studies that show this hasn't improved. It's very subjective because it's the surgeon in the mix, right. When it's the human in the mix, it's like saying will you drive without your navigation system? Will you just close your eyes trusting the navigation system? No, you wouldn't.
- 00:20:41 So, it all depends on the experience of the surgeon. Obviously the younger surgeons use the navigation system more. They know it better. The older surgeon goes in, he's talking to me about his day. And I say, "How do you know there's a tumor there?" He said, "It's intuition. I know it feels different." And I wouldn't want him to be any different because he was trained without this. So, the only thing he

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knows is he looks up and he says if I go further,  
there is an [unintelligible] right there.

00:21:10      How much further? That's not important to him. All  
he needs to know is if he turns left, you will lose  
language. So, he is not going to go there. And  
that's about it. And there have been animal studies  
which show the validity of DTI [ph.] or your of all  
of them, but every time you change the tracking [ph.]  
involved [ph.], then you have to run the animal  
studies all over again.

00:21:33      There are studies about the cortical stim. When you  
do motor, you can actually stim your exactly there  
and say whether - and that's what we do. So, all our  
tracking is validated against stim, which means a  
hand track is there. You stim the brain. Can you  
move your hand still? No, you can't. Your  
tractography was correct. But this you're talking  
about in a region of almost like three millimeters  
accuracy. So, that's about all they need for their  
navigation.

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- 00:22:12 MALE: Does the visualization include any sort of uncertainty communicated - uncertainty of the model fit if there is enough - you know, does a fit sometimes are better than other times of the model? And is that communicated in the visualization to the doctor? So, would that be useful to communicate that?
- 00:22:31 RAGINI VERMA: That is very useful. I mean that's something which we - it's very difficult to validate. So, we do give them a map of the uncertainty in the brain because depending on your tracking algorithm, if you're doing streamline tracking, two different kinds, the deterministic and probabilistic tracking. Deterministic means every time I know there is this way to get from here to that door. Probabilistic says I'm going to stand here and I'm going to try and see if I can go this way maybe with a lower probability. It will give me more time. This is one way. That's probabilistic.
- 00:23:04 You can get that uncertainty mapped for surgeons and they actually like it, but there is not much in terms

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of combining the probabilistic with the visualization  
of the track.

00:23:17 LYNNE PADGETT: Great. Okay, Dr. Verma, thank you.  
No. No. I did call you by the right name. Sorry.  
I apologize. Thank you for that and the great  
discussion and questions. Clearly I think that set  
the tone for the day. So, I will invite the next  
presenter to come up. And while you're setting that  
up, I am going to relay a message from Donna that is  
going to be content-driven, but I'm not exactly sure  
how to do it.

00:23:43 So, however, for the quality of the webinar I'm  
assuming, when you're showing your PowerPoint slides,  
make sure that you're - from the laptop, make sure  
that the resolution is set to 1028. So, and I'm just  
going to go ahead and while we're getting this set up  
and set the norm for the rest of the moderators  
because I'm first, right, so I can do that.

00:24:08 We'll be distracting your visual field right out  
here, okay. So, when you see the signs come up,  
that's what it is. There is a small series of foot

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shocks that will occur if you go - no, I'm teasing.  
Not really. So, but thank you. I just wanted to  
kind of cue everyone, behaviorally cue them, like the  
good behaviorist I am, to where to look or where to  
ignore. And we'll keep things going on time. This  
has been very exciting. So, thank you, and I will  
now shift it back over to the people who actually  
have the knowledge.

00:24:46 NICK TURK-BROWNE: A lot of pressure. So, I'm  
sticking by Todd's one-slide rule but using a lot of  
animation. And I'm not going to talk about medical  
imaging or visual search, but what I am going to tell  
you about is something that I hope you'll see is  
connected to those topics.

00:25:10 So, we've been interested in my lab for a while in  
the idea of temporal context. And temporal context  
is an idea from the memory literature. The idea is  
that when you experience something, the way it gets  
recorded in memory is not just in terms of the  
details of that experience, but it's also with  
respect to other things you've seen recently, what  
you're thinking about, what you're doing, and so on.

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So, we don't store memories in a kind of isolated way. They're embedded in this ongoing buffer of recent experience.

00:25:41 And so we've been interested for a while in the idea that maybe the way the visual system encodes stimuli is also contingent on temporal context. And so the example here is the scene C - that's confusing. And the idea is that when you are looking at the scene, you saw other things recently. So, you might have seen a theater or a forest scene. And the question is does the way your visual system encode C depend on what you had seen beforehand?

00:26:11 So, the way that we went about trying to get at this was using a technique known as repetition suppression. I realize most people may not be familiar with that. It's basically the idea that parts of the visual system that code for a stimulus respond less when the stimulus is repeated versus novel. And insofar as scene-selective cortex, the parts of the brain that encode scenes, store our scenes with respect to their temporal context, then

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the stimulus repetition should be better if it's  
embedded within a repeated context.

00:26:42 That is if a visual region encodes temporal context,  
then repeating those aspects of the experience should  
leave a stronger repetition suppression. So, this is  
basically the kind of experiment we did. People were  
making indoor/outdoor judgments on these scenes. And  
so they would see one at a time and then a few  
seconds later another and so on.

00:27:01 So, they were doing a cover task unrelated to this  
context manipulation. Later on in the experiment  
they would see the same images again. So, this was  
done in an fMRI machine. And what I'm going to show  
you here is the data from scene-selective cortex, the  
parahippocampal place area, part of parahippocampal  
gyrus [unintelligible] that seems to respond  
preferentially to pictures like this.

00:27:28 Okay. So, after some period of time there's going to  
be some repetition here. And so there's two  
conditions, two critical conditions. I might  
experience the same context again. And our

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hypothesis was that this would allow you to kind of generate an expectation of the subsequent scene, for example some kind of implicit prediction like this, that might explain away or potentiate the representation of that item such that you would get greater repetition suppression if it actually appeared.

00:27:58 And we contrasted this with a case where - oh, I guess I'll show you the data here. And so the basic effects [ph.] is that if you look at the solid line, that's the response to C - three minutes left? Okay. And so if you look at the solid line, that's the response to C when it's novel, the dash line is the response to C when it's repeated.

00:28:24 And so you see the decrease in the response in scene-selective cortex is this index repetition suppression. And the critical question is what if you experience the same C scene, but it's preceded by other items in the sequence several seconds beforehand and so you don't really have any expectations going into the perception of C, and in fact, what we found is that you don't get strong



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repetition suppression in this case, and there's a significant interaction here, suggesting that there's a better representation of C in the case in which it's been embedded in the same temporal context.

00:29:00 I'm only going to talk to this control experiments here, and then I'd be happy to answer questions about it. Okay. So, we don't actually know that there's prediction going on here. It could be some kind of hysteresis in the visual system if there's kind of - the way in which you encode C is kind of state [ph.] dependent or context dependent. So, how do we know that these repetition suppression effects due to repeated temporal context relate to prediction?

00:29:23 So, we've been using in a series of other experiments - I'll tell you about one flavor of this. We've been using fMRI again to kind of try to decode what people are predicting on a moment-by-moment basis. And so the design of these experiments is a little bit different. So, you have A followed by D followed by F, and F is a face here. Oh, that's just a coincidence. The letter F was the next letter in the alphabet.

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00:29:47 And the idea is that when the context is repeated in the future insofar as people are generating a prediction of S [ph.], we might be able to decode that using multivariate analysis techniques. At a categorical level we can look at how much classifier evidence there is for faces coming to mind. And the particular experiment that I'm talking about here as the case were insofar as this prediction is happening, the prediction is violated.

00:30:12 And the dependent measure here was subsequent memory for the S [ph.] item. And so if you're predicting S [ph.] and then G happens, the idea is that this prediction error [ph.] might be a way to kind of update memory, that F is not a reliable part of this context because it initially appeared there, but now it doesn't appear. And so we're measuring kind of subsequent memory for the F item as a function of the strength of the prediction for F when A and B are presented.

00:30:40 So, just to show you the final thing here, again, the dependent measure here is subsequent memory for S

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[ph.], and we're going to relate that to the classifier evidence for S [ph.] in the repeated context. Critically there's no face presented in the repeated context. So, any evidence for face information can be interpreted perhaps as evidence of prediction.

00:31:00

So, the main point here is that we actually can decode really reliably that people are predicting at least the category of F [ph.] when A and B is repeated. We've done representational similarity analyses as well. We can decode that you are in fact predicting this particular face when A and B are repeated, amongst other faces. And the finding in this study was simply that the more strongly you predict F when A and B are repeated, the more likely you are to forget F later on when your prediction was violated.

00:31:27

And so this is just showing classifier evidence on the X axis. The more classifier evidence there was for F, the weaker your memory for F later on when the prediction was violated. So, I think I will stop

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there, and I'd be happy to take any questions.

[applause] Yeah?

00:31:49 MALE: If you add the time variable in addition to the serial order variable, how predictable does this paradigm remain?

00:31:59 NICK TURK-BROWNE: Yeah. So, in this case the timing was jittered for my analysis reasons, and so there was no actual kind of time regularity. It wasn't the case that C occurred three seconds after B. I would expect that if you built that kind of regularity into it, that you'd get a stronger effect, but the problem is if you have kind of structure in the timing of events, it's hard to deconvolve [ph.] the hemodynamic response to individual events. And so behaviorally you see evidence that when the timing is predictable, you get stronger priming effects and other kinds of things.

00:32:31 MALE: So, the time variable was just in the model as a nuisance variable?

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00:32:36 NICK TURK-BROWNE: Well, it's set up to reduce the covariance of the regressors for the items. And so the idea is it varied between three and six seconds I think. So, it wasn't a huge amount of variability, and it was just so that we look at the response to individual items.

00:32:54 MALE: Remind me, the task, how does the task modulate this effect, whether they're doing a passive viewing or they're engaging, you know, whatever. Yeah.

00:33:04 NICK TURK-BROWNE: Yeah. So, all of these experiments during the phase in which we're looking for either repetition suppression or prediction effects, they're doing a covered task of these categorization judgments. And so it could be in that first case, indoor/outdoor judgments. It can be [unintelligible] category. So, for the later cases where we have scenes and faces, you might be saying whether each stimulus is a scene or a face.

00:33:26 We haven't done passive viewing, partly because we wanted a behavioral analog of some of these effects.

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You do get response time benefits when items appear in repeated context consistent with a kind of predictive idea. I think the fact that the stimuli are past-relevant is part of the story. I don't know if you would get it if they weren't attended or if they weren't past relevant. Yeah?

00:33:51 FEMALE: Is that on? Oh. I'm wondering about the time scale of this. I know that some of these are in the order of seconds. Were there implications for, for example, interweaving tasks of reading different image types and things like that, you know, if you were like hours, days, et cetera, rather than seconds?

00:34:10 NICK TURK-BROWNE: Yeah. So, the time scale of temporal context effects has been studied extensively in the memory literature, but there's actually very little work on that in vision that I know of. We start seeing in the second study where we're looking at prediction error, but the real point I want to mention in that studies is that we start being able to decode what you're predicting at the A item. So, almost immediately when you get a predictive cue.

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00:34:40       What the range is about how far back in time you can go in terms of binding prior items to the current experience, I'm not sure. It's an interesting question. Yeah?

00:34:51       MALE: So, how do I use this information to help clinicians make better decisions or...?

NICK TURK-BROWNE: Gosh, I wish I knew.

MALE: ...design a study...

NICK TURK-BROWNE: Yeah.

MALE: ...or to design studies that can have better ability to evaluate an imaging modality?

00:35:06       NICK TURK-BROWNE: So, yeah, I thought about this when I was making my slide. How can I relate this clinically? I think that, you know, so context is not something that's taken into account my guess is in some of these, you know, medical image reading activities. So, the suggestion here would be that there's some kind of history effect that what you were just doing before or looking at - what application are you talking about, just before I go out on a tangent?

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00:35:39 MALE: So, we review all types of imaging devices.  
The prototypical...  
MALE: It's for the FDA.  
NICK TURK-BROWNE: Okay.  
MALE: The prototypical evaluation or the most  
studied imaging modality is probably mammography  
where you have a mammographer sitting at a  
workstation looking at mammography images for four  
hours straight...  
NICK TURK-BROWNE: Right.  
MALE: ...with a break or something. And so how does  
that workflow or a study designed to evaluate that  
workflow...  
NICK TURK-BROWNE: Yeah.  
MALE: ...how can that be impacted?

00:36:08 NICK TURK-BROWNE: So, I think one idea is insofar as  
their ability to detect a tumor in an image or  
insofar as the way they're representing the current  
image that they're looking at is contingent upon  
other images that they saw recently, you can imagine  
that you would get biases of the order. So, if there  
wasn't anything notable on a previous image, that



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might bias you to be less likely to see something in  
the current image.

00:36:33 And in terms of prescriptions, I'm not sure. I don't  
know how people look at these kinds of scans. Do  
they look sequentially through the images in a  
particular order?

00:36:44 MALE: Two of them will come up at a time for the  
different projection angles.

NICK TURK-BROWNE: Right.

MALE: And then there's two breasts obviously. And  
so that's a presentation paradigm. And you're right,  
they see about 95 percent, 90 percent are normal.

NICK TURK-BROWNE: Yeah.

MALE: And so they look at these images for a minute.

NICK TURK-BROWNE: So, how many slices? They only  
get two slices per breast?

MALE: Two views.

MALE: It's a projection...

NICK TURK-BROWNE: Two views.

MALE: Basically it's a project image, although 3-D  
imaging is coming and is there in some hospitals.

NICK TURK-BROWNE: Yeah.

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00:37:19 MALE: Brian, if I can - I can pick up on that. It might be that this is an argument for having like a consistent hanging protocol because it would give you some sort of perceptual fluency. You know that this is coming up and this is coming up and this is coming up. I don't know that anybody would have any evidence that it would change accuracy, but it might change the fluency with which somebody moves through the imagery. [inaudible] could imagine that.

00:37:49 NICK TURK-BROWNE: So, some of the theoretical context for this kind of work is we're kind of inspired by models of predictive coding, the idea that at any moment what you represent is kind of the difference between what you could have expected coming into that moment and what actually happens. And insofar as you have a prediction based on prior experience, that might highlight unexpected things, tumors and so on. So, I don't know if that's actually going on, but you can imagine that insofar as the visual system is representing deviations from expectation, setting up some kind of [unintelligible] might highlight unexpected things more?

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00:38:24 MALE: Or alternatively it would work in exactly the opposite direction and you would - in an intentional blindness kind of a way...

NICK TURK-BROWNE: Yeah.

MALE: ...you would see what you expect and not pick up the deviation.

NICK TURK-BROWNE: Yeah. It's a really interesting issue in that literature. There's two views about this, whether what predictions do is kind of explain away expected information so that it highlights unexpected things. And the other view is that predictions set up kind of a filter through which you experience predicted stuff and you filter out unpredicted stuff. So, you'd become more blind to unexpected things. And there's evidence in different domains for both of those kinds of effects.

00:39:07 MALE: Yeah. I'm just trying to sort through the difference between predictive coding and the brain somehow trying to represent emotion out in the world. So, in computer vision as that field sort of moves from images to a video...

MALE: Movies.

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MALE: ...they're finding great importance in thinking of their old image-based features over time. They are coming up with spatiotemporal features.

NICK TURK-BROWNE: Right.

00:39:38 MALE: All right. The brain doesn't know that it's being presented with these random sort of images one after the other. It's used to seeing other emotions out in the real world, and [unintelligible] developed features that is looking for how these things change over time. Those same features might be in play here.

NICK TURK-BROWNE: Yeah.

MALE: Is that predictive coding? Is it something different?

00:39:58 NICK TURK-BROWNE: Yeah. I think it's a really interesting question. You know, we kind of went to a boundary condition here where they're totally random and not only random in term of the images and the order, the initial order, but the category of the images and so on. So, this is very from an everyday spatiotemporal experience perspective, this is very atypical. But you're right that that doesn't mean

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that the brain isn't trying to do that kind of spatiotemporal extrapolation and that that's the source of these kinds of predictive effects.

00:40:29 You could look at that I think if you build some visual similarity into the transitions to see whether you get bigger effects, if there's some kind of relationship between the images. My guess would be that there would be. I guess is the question about motion or is it about trying to make sense of the sequence of what you're experiencing?

MALE: Well, one probably comes back to the other.

NICK TURK-BROWNE: Yeah.

00:40:51 MALE: So, I mean I think it would be the case if you essentially had your experiment where over the frames it would create some sort of lower [unintelligible] of motion in some sense to see whether that changes the effect that you're observing.

00:41:08 NICK TURK-BROWNE: Yeah, it's an interesting question. The other thing we've thought about in that context is morphing the images one into another so it's more continuous. Yeah.

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00:41:17 MALE: I was going to say kind of related to this, is this...

LYNNE PADGETT: [inaudible].

MALE: When you get this prediction, is it limited to the exact image or is it across categories? I might have missed that.

NICK TURK-BROWNE: Yeah. So, I rushed through that.

MALE: If you get a Grand Canyon image, so we pick this, this, then I get a canyon, does it have to be the exact same image of the Grand Canyon...

NICK TURK-BROWNE: Yeah.

MALE: ...or would we still get this effect for the same category but different image?

00:41:42 NICK TURK-BROWNE: Right, a different - well, right, so there could be a gradient of specificity, other Grand Canyon images, right, versus just canyons in general versus outdoor scenes and you could look at kind of the level of representation of these predictions. In terms of the second study where I actually tried to measure anticipatory information about stimuli, we set up the experiment so that the thing you were predicting was the opposite category

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from what you were looking at, and that was just to hit it with a hammer, you know, to find something different.

00:42:12 But we did do these item-based analyses where essentially you can look at whether the pattern of information that comes to mind during the repeated context matches what you saw - the pattern of activity - when the context [unintelligible] matches the pattern of activity that was evoked by the stimulus itself. So, when you see the Grand Canyon, we get an index of how that stimulus is represented and then we can say is the pattern of activity elicited when the context repeated the same?

00:42:36 And the critical test there is like a permutation test. You ask is it more similar to that scene relative to this full set of other scenes? And so we do find those kinds of effect. I think so it's item-specific, but that doesn't totally answer your question because the space of items is so broad you don't know about how precise their representation is. I think that's a very interesting idea.

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00:43:02 MALE: So, it seems to me Ragini Verma just gave a perfect example of contact-based visual prediction when she said an experienced surgeon looks at that MRI or whatever, [unintelligible], and says I'm going to stop here. So, context-based prediction happens in medical imaging. The question is how is the - what are the features being used and how is the surgeon using them?

NICK TURK-BROWNE: Yeah.

00:43:33 MALE: And I think that's where from the medical imaging perspective that's the real challenge is figuring out those two things.

00:43:41 NICK TURK-BROWNE: Yeah. I think it's a really - just go back a little bit to Jeremy's point that you could imagine that if your goal is to make a surgeon or a radiologist maximally sensitive to information in the current moment, it might be better or best to scramble their experience going into that moment so that they can't block it.

MALE: Whoa.



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NICK TURK-BROWNE: I don't know. I'm not a surgeon.  
But what context are we talking about here? Are you  
actually talking about surgery?

00:44:07 MALE: Yeah. Her presentation was on surgery.

NICK TURK-BROWNE: Yeah.

MALE: They look and they got to decide how deep to  
cut.

NICK TURK-BROWNE: Yeah.

MALE: They're looking at the image and saying I'm  
going to cut this far and I'm not going any  
further...

NICK TURK-BROWNE: Yeah.

MALE: ...and I maybe can't even tell you why, but  
just my experience tells me I'm not going any further  
or else I incur some damage. And that is prediction.

NICK TURK-BROWNE: Sure.

MALE: So, the phenomenon is operational. The  
question is...

NICK TURK-BROWNE: What is it?

MALE: ...the mechanics of it.

00:44:32 And I think those are really interesting questions,  
but I think that's a challenging thing to try and

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study in that context because it's not like you can't go out to Google and get a thousand images so easily or something like that. You have to carefully consider how you curate your stimuli.

00:44:48 NICK TURK-BROWNE: Yeah. And it goes back to the previous question about is some structure in the image of themselves over time in that case too. It's a domain that I haven't actually thought a lot about. One to note here is that these kinds of predictive effects are implicit; that is that people don't really - they're not aware of what's coming up next. We're kind of measuring that in the background of some other tasks they're doing. And so how that relates to some intuitive sense of knowing what to do next in that case of the surgeon I think is an interesting question.

00:45:21 The neural mechanisms of this I understand a little bit more and I can explain if that's relevant, but that kind of [unintelligible] that understanding the basic science mechanisms of prediction. And so I think there's kind of a more applied question about what is the effect of prediction in these contexts,

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how important is it? I agree with your intuition  
that some amount of prediction is happening when  
you're trying to act based on limited information.

00:45:53 FEMALE: So, I guess another aspect of that is when a  
radiologist reads, so where they're going through one  
image after another image after another image, if  
there is a prediction thing, then maybe the  
radiologist should read all brain tumor images  
together in the morning and not go from MS to brain  
tumor to any other kind of lesion if there is no - I  
mean it depends, but I don't know.

00:46:21 NICK TURK-BROWNE: Yeah. So, it comes back to this  
question of whether prediction blocks out unpredicted  
stuff versus prediction allows you to detect  
unexpected things.  
[inaudible response from audience]

00:46:36 NICK TURK-BROWNE: Oh, I'm completely unconcerned  
with practical matters here.  
[inaudible response from audience]

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00:46:56 NICK TURK-BROWNE: Are there any studies on this, whether people have a specialized domain of radiology versus their generalist?

FEMALE: Well, [inaudible] repeated [inaudible] depending on what [inaudible] and, you know, the business of health care [inaudible] radiology [inaudible]...

NICK TURK-BROWNE: Everything.

FEMALE: ...[inaudible] what to do. Then you have to sort of - the breaks I think are the more important ones for [inaudible] taking a break or not just to get a sense - and most people want it [inaudible].

00:47:28 Some of the things we read in nuclear medicine [inaudible] very low [inaudible] activity. So, it's [inaudible]. It takes [inaudible] time. You have to take a break after [inaudible].

00:47:58 So, I think people instinctively know [inaudible] breaks or not [inaudible].

NICK TURK-BROWNE: Right. You could do this in mammography, for example. I mean one of the confounding factors in mammography is the background complexity of the tissue. As you get to what we call

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denser breasts, it's harder to detect answers. And there are algorithms today that would automatically determine the amount of density.

00:48:25 So, we could do an experiment where we could go from low-density breasts to very high-density breasts in a gradient over the morning, you know, so that you're progressively getting harder breasts or the other way around perhaps if you're worrying about fatigue, or we could interleave them, you know, high density, low density, high density, low density and actually look at that.

00:48:45 MALE: That's a really interesting question, interesting designs we could do there.

NICK TURK-BROWNE: Yeah. I didn't talk about it, but a lot of the work on my lab is on statistical learning I do to extract regularities across experiences. And this is exactly the kind of thing you might imagine. If you give people a foothold and you ramp up the difficulty, I don't know. I mean in some context that improves performance.

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00:49:03 MALE: Well, there is some analogy in the British system. So, the British system has a two-tiered reading. So, they have a set of readers that have a very high sensitivity. So, they all read the cases and maybe point out 20 percent. And then those 20 percent go to a high specificity reader who then tries to discern in this [unintelligible] population. And they hence seem to work better than we do in the general population.

00:49:31 NICK TURK-BROWNE: There's very relevant literature [ph.] if you haven't explored it, on perceptual learning and how you acquire perceptual expertise in these domains. We don't all kind of star at visual search. [unintelligible] we acquire expertise over time. And I could imagine things like this, whether you're a generalist or whether you're specialized for certain kinds of images, you could be better or worse depending on the nature of the learning. And maybe these high-sensitivity people have more perceptual learning. They learn to make more subtle distinctions in the images.

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00:50:01 MALE: A useful [unintelligible] given this particular audience is that the medical community uses sensitivity to basically mean hit rate and the psychophysical community uses sensitivity to mean [unintelligible]. We can end up with interesting confusion if we do not keep that in mind.

NICK TURK-BROWNE: Do you speak from experience?

MALE: You betcha.

00:50:19 FEMALE: I'm going to jump in, Craig. So, I wanted to pick up on this idea of having to read different type of images, marrow images, cancer images. You take what comes to you and [unintelligible] context based. And I'm wondering if a radiologist knows that he or she needs to focus because hey, I'm switching from a cancer image to a psych image to an MS image, does that increase the attention? What is that role of self-regulation on behavior as you come into that task? I think that's another important question.

00:51:00 NICK TURK-BROWNE: So, the relevant cognitive literature here is on task switching. Factories are set up in assembly lines because people are good at doing the same thing over and over. And so there's a

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whole literature on how people do task switching and the difficulty of it and the conditions under which people can switch better between doing different things and so on.

00:51:22 MALE: And how much uses a medical imaging reading background or application? [unintelligible] this whole field needs to do is start actually interacting in the medical field so that they can tune their experiments to be much more relevant to the medical imaging task and workflow.

00:51:46 MALE: Can I say something too? There is literature on this in radiology, at least for mammography...

NICK TURK-BROWNE: Right.

MALE: ...with batch reading versus point of service kind of things, which are different, and it's pretty mixed and it's pretty hard to get answers. I've looked at sequential correlations in mammogram reading, and I can't find anything significant.

NICK TURK-BROWNE: Okay.

MALE: But that doesn't mean - that's maybe a power issue.



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00:52:08 NICK TURK-BROWNE: So, by batch you mean you do a lot of them at the same time or...?

MALE: You read a bunch of mammograms all at once as opposed to you taking what you get. If you're a community-based radiologist, you may not have the luxury. You may only have a few mammograms to read today.

NICK TURK-BROWNE: Right.

MALE: And you may have one or none or - and so you may have to just mix as it is. But the results on that were pretty mixed. The recall and detection rates at least don't appear to kind of go in either, you know, can go in any direction.

NICK TURK-BROWNE: Interesting.

00:52:37 MALE: Another thing I'd point out. I don't think of that so much as prediction anymore. That's adaption.

NICK TURK-BROWNE: Oh well, yeah. They've very related.

MALE: So, prediction is when you're using information from those to - there's a connection there.

NICK TURK-BROWNE: Yeah.

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MALE: And the reason it's predictive in your case is because you've seen those before and you know what comes next.

NICK TURK-BROWNE: Yeah. Yeah.

MALE: And in the case of the brain surgeons, the brain surgeon has seen those [unintelligible] before and is saying okay, if I go much further than this, there's going to be a bad outcome...

NICK TURK-BROWNE: Right.

00:53:05 MALE: ...as opposed to just randomly you happen to see these two things and do they affect you. That to me is more a question of adaptation and less one of predicting.

00:53:14 NICK TURK-BROWNE: Yeah. That's a - I won't go into it right now, but we could talk more about it. There's a really interesting connection between prediction and adaptation. Yeah.

00:53:34 MALE: Okay. All right. Yeah. [unintelligible] there is a distinction between a prediction and adaptation, but I was actually going to put those into the same category and contrast this with a

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question of visual search, whether you should sort of group together your searches of a particular category or not. Ultimately what this boils down to is that you want to try to tune up your classifier for a particular category of image, whether it is MS or a mammography.

00:54:12 So, you want to sort of - you don't want to keep switching back and forth between these different sort of categorical templates.

NICK TURK-BROWNE: Yeah.

MALE: [unintelligible] keep one going so that you can [unintelligible] your classifier over the course of maybe several instances of viewing.

00:54:28 NICK TURK-BROWNE: Yeah. It's an interesting question. Is there literature on this [inaudible]?

MALE: The difficulty with that in radiology I would think is that unlike in our lab tasks, you tend to be looking for more than one target type at a time. Even if you're doing a restricted task like mammo, you're going to be looking for calcifications and masses and architectural distortions, and you can't really imagine that what you're doing is the, you

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know, tuning up your teddy bear detector in quite the same way.

00:55:04 So, this is actually probably a good example, but Craig's talking about where what we really need to do is do a collection of lab-based experiments where the situation is a little closer to what radiologists actually face where you're dealing - so, you're dealing with a complex target to start with and then you're supposed to look for incidental findings just in case the guy actually has pneumonia to boot.

00:55:31 MALE: Well, this is the problem because I don't know what this target is. I don't know if it is a single target. The target is cancer.

MALE: Is that a...

MALE: Well, we know in terms of...

MALE: If it's multiple targets, then let's get exemplars of the different multiple targets and train up these separate sort of sub-classifiers.

MALE: It sounds like a random, you know, what's the CAD system looking for? You just can't - I don't think there's any good evidence that you can have a single perceptual template that is cancer any more

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than you can have a nice template at the airport that  
is threat.

00:56:09 NICK TURK-BROWNE: Well, that's an interesting  
question in my mind whether you can kind of learn  
about the distribution of targets, right, and given  
variable experience in a diverse target set, can you  
actually learn something about this diversity? I  
mean it's not totally random, right? You know what  
to look for in a general sense.

00:56:26 MALE: Yeah. Well, we know from stuff that we've  
done that radiologists seem to be able to use the  
overall texture of the breast for instance to say  
it's more likely that there's something going on here  
in this breast than in that breast. In that sort of  
sense there's clearly some sort of perceptual  
learning here. This is not to say that the stuff  
that we - that sort of the classic research  
literature has done is in any way irrelevant. We  
just need to scale up the problem...

NICK TURK-BROWNE: Yeah.

MALE: ...to be closer to the radiology problem.

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00:57:02 MALE: There are actually many studies that have investigated humans searching for a single target hearing a single signal embedded in a computer-generated noise...

MALE: Multiple target.

MALE: ...background versus - yeah. That's something like 180 or, you know, the uncertainty shape of the target. When you actually compare it under conditions where you can actually compare it to [unintelligible], humans are actually more efficient, meaning that they actually are better when there's uncertainty than when there's a single target they're looking for.

00:57:33 And that's because even when humans are instructed to look for a single - you're shown the picture and that's a single target that can actually occur with a little [unintelligible] shape, often humans behave as if they actually have some uncertainty. So, they're actually using multiple templates [ph.] even though they should be using one. When they actually humans are already doing that, which is what the [unintelligible] they're using multiple templates [ph.], and they're actually more efficient.

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00:58:00       And there's I'd say maybe - I don't know there are a lot studies on the different circumstances. So, humans, even when you tell them already for some reason that there's a [unintelligible], they behave with some uncertainty and partly because, you know, at least many of us speculate...

MALE: Thank you, Lee [ph.].

MALE: ...had to do because in real life things are not fixed. They have uncertainty. So, the brain sort of takes into account as representations or, you know, there are sort of variants [ph.] [unintelligible].

00:58:25       LYNNE PADGETT: So, it hurts me to interrupt for a couple of reasons. One...

NICK TURK-BROWNE: Do I get to respond?

LYNNE PADGETT: No.

NICK TURK-BROWNE: Oh.

LYNNE PADGETT: I'm sorry. [laughter] I'm sorry. And that's why I'm moderating instead of Todd. You can respond, just not right now.

NICK TURK-BROWNE: Okay.

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00:58:40 LYNNE PADGETT: So, what I'd like to do is sort of, one, indicate how successful the meeting is already going. I see research questions. I see links. I see lots of important thoughts and connections happening. So, that's very exciting. I'm sorry that because that happens I have to step in and say let's shift to our next speaker so that we can add new, exciting, and more complicated topics to this. So, why don't you come and go ahead and get your stuff going. The rest of you can murmur quietly and go, "When does she sit down and the next moderator come up?" So...

00:59:23 ANDREW MAIDMENT: So, while Todd sets up his laptop, I'll just tell you I had presumed that there were people in the audience who might not know what mammography was, and I'm glad I did that. I'm going to give a very brief overview though of breast imaging and a little bit of how we're using vision research to design imaging systems. And the target [ph.] for this will be breast tomosynthesis.



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00:59:57 LYNNE PADGETT: I would take this moment to say that when you're not talking [unintelligible], but when you're not talking, be sure and turn the mic off.

01:00:13 ANDREW MAIDMENT: All right. The other thing I presumed was wide screen. So, it's going to be a bit interesting to see how this fits.

01:00:27 All righty. There we go. So, in breast - so, in mammography what we do is a single projection of the breast. We do it at different angles and we do each breast individually. But we do a single projection of the breast. We're making a two-dimensional image. Mammography has probably in some sense peaked. The technology is such that we are generating three-dimensional images, and we're doing it with a form of computer tomography that we colloquially call tomosynthesis.

01:00:57 The idea of tomosynthesis is that the x-ray tube moves around limited range of angles so that we can mirror the geometry of mammography, having a compressed breast held some distance from the x-ray tube, but we're only moving the x-ray tube over a

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very limited range of angles. And each manufacturer has a slightly different approach. The results are these tomographic slices. They're not perfectly isotropic in a three-dimensional sense, but they have a lot of good qualities in terms of their ability to separate structures and depth.

01:01:27 And so here you have an example of the same tumor in mammography and in tomosynthesis. And what you have is that the mammography has a very complex background that is affected by all the structures that are above and below it, and it can create a sort of [unintelligible] of tissue that obscures the tumor. Whereas, when you remove that [unintelligible], the tumor is portrayed rather graphically.

01:01:50 And I think most of you would agree that you could see a tumor in the tomosynthesis image; whereas, I think most of you might be scratching your head a bit in the mammography, especially that I've sort of cut down the field of view a little bit. Now, there's lots of evidence that suggests clinically that tomosynthesis improves upon mammography. There's a bit of a caveat here because of the way we're

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actually doing tomosynthesis today as an adjunct to  
mammography.

01:02:15 But in the ROC curve you see that in this study with  
15 readers and about 400 patients from Elizabeth  
Rafferty at MGH, you get a statistically [ph.]  
significant improvement in the ROC curve for the  
addition of tomosynthesis. In our own clinical  
practice at the University of Pennsylvania, we did an  
observational study comparing screening in patients  
with mammography to screening in patients with  
tomosynthesis. And we get about a 25 percent  
reduction in the callback rate, meaning that there's  
25 percent fewer women that have at least something  
suspicious enough for us to do more imaging.

01:02:49 And our cancer detection rate has increased about 25  
percent as well. The second one not statistically  
significant; the first one is. So, it's not just  
that we're not calling back as many women and we're  
not seeing as many cancers; we're calling back fewer  
women and we're seeing more cancers. The problem  
with tomosynthesis is if you look at sort of subsets  
of cases, there's really no improvement in the

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detection of cancer of cases that are determined by calcifications only.

01:03:16 So, calcifications are small secretions of calcium that occur naturally in the breast but are prevalent in certain types of cancers. So, the improvement is in non-calcified cases, not in calcification-only cases. So, what we did is we looked at ways to design a new imaging system, the next generation of tomosynthesis systems. And what we came up with is a design that had a novel x-ray tube motion and a novel detector motion that actually improved the image quality of calcifications.

01:03:50 And I think you can see in that image that they're sharper, there's more detail, there's a greater number of calcifications that's visible. And this gives us a principle of super-resolution. But what's interesting I think for this group is how we did that. We did that with what we call a virtual clinical trial framework. And I'm in some sense a bit of an integrator. I take things from different fields and pull them together. And so what we've done is make them two pipelines.

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01:04:14 The first one that simulates patient recruitment, patient imaging, and data archiving, which we've replaced basically with phantom simulation, phantom imaging, and data archiving. And then we take it a second pipeline from Barco, a medical monitor company that would in some sets. And the second phase of imaging quality had the [unintelligible] study, right. You'd have the image display, human interpretation, and some statistical analysis, and we replace that by this pipeline of display simulation, visual system simulation, and the machine observer.

01:04:45 And so the net result is that you get images like this with objects embedded in them. You have [unintelligible] related to the detection of them. And for example, this is just one of the many studies that we've done, this one in collaboration with the FDA, where we were to sort of look at operating regimes of detectors and sort of what sort of dose you'd use for that and what sort of noise you would allow in your detector.

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01:05:07 But the previous system, the super-resolution, the next-generation tomosynthesis system, the design and the validation was all done in silica (?). We discovered that super-resolution occurred through virtual clinical trials. We then used them to sort of develop new imaging systems and to optimize that design.

01:05:28 And this is a last quick slide. Where is it going? We're adding functional information at this point. So, this is a contrast-enhanced tomosynthesis study I think of one of two systems in the country right now that are doing contrast-enhanced tomo. This one's at Huff [ph.]. And you can see the first image is an anatomy image. Then you have an arterial phase image, a venous phase image, and a late enhancement image basically showing uptake of contrast-enhanced by a tumor.

01:05:55 The clip shows you what we thought was a tumor in fact was the whole breast. What we'd like to do is move towards temporal, getting temporal information. And we do that by basically [unintelligible] system to do a slow scan. And this is a graphic. This is a

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tomographic slice through a phantom showing you the inflow and outflow of contrast agent over time at essentially the same radiation dose as current 3-D systems.

01:06:23      What we're working towards now is adding contrast agents, new developments like that, to sort of improve our functional information. So, everything we're doing is trying to reduce the complexity of the signal to try to improve our ability to detect cancers quickly and efficaciously. That's it.  
[applause]

01:06:46      MALE: In your, the tomo study in your clinic, do you have a feeling for whether or not tomo increased the amount of time per case and by sort of how much?

01:07:00      ANDREW MAIDMENT: So, we didn't specifically study that. I can tell you it takes a little longer. It's not an enormous amount longer. It's probably about 30 percent longer or something of that, about 20 to 30 percent longer. There's more images to look at, but you look at them fairly quickly. You look at them in a stack [ph.] mode and you scroll through

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them. And you use - there must be some sort of clue in that sort of temporal sequencing that we call it the pop-out [ph.] effect that, you know, things sort of laugh at you. But yeah, it's longer.

01:07:29 And part of that is because of the fact that the way it was approved, we have to read the 2-D image and the 3-D image. So, you intrinsically are having to look at more data. We are working towards reading 3-D only. And for example, the new GE system that was just approved a couple weeks ago, that you can look at the 3-D image. They're allowed to look at that. A lot of this has to do with what the FDA has - or in fact what the manufacturer has gone to the FDA to ask for approval in. There's a reading sequence that they have to follow, the readers have to follow.

01:08:10 MALE: I was basically at the model observer that led to the probing and the development of the imaging, was that 2-D or 3-D?



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01:08:21      ANDREW MAIDMENT:    So, that's a 3-D CHO following  
                                 Olivia Blitz (sp?) work, and I think it's the type  
                                 two observer of hers.

01:08:31      MALE:    And then so for everyone else, these are not  
                                 the most complicated models in the world. They don't  
                                 model everything that's going on in the human  
                                 observer. They're very linked to contrast and  
                                 structure, but not so much a lot more than that. So,  
                                 these are basically templates that do some background  
                                 correction for the correlations in the background and  
                                 then they stick hot spots or the looking for what  
                                 you'll find, and that's the calcifications or tumors.

01:09:05      And so that model development you all would probably  
                                 find is the most trivial. And why did they stop  
                                 there? They stopped there because it adapts well to  
                                 different environments, and it's very fast to get to  
                                 performance metrics for phantom images. And I think  
                                 that kind of helps make that translation for  
                                 everybody. It's been very effective. We've also  
                                 seen these kind of model observers to get FDA  
                                 approval of [unintelligible] language saying that my  
                                 reconstruction method now works at lower doses. That

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was all based - some approvals have been based on  
model observers with no humans even part of the  
clinical study.

01:09:51 ANDREW MAIDMENT: In our work what we've done is sort  
of concentrate on this human visual system and adding  
details into the human visual system.  
[unintelligible] that's sort of what's presented to  
the CHO. We've not done a lot of development in the  
CHO.

01:10:09 MALE: One of the things we're seeing is when  
radiologists actually look at 2-D mammograms, one of  
the things [unintelligible] makes the task very  
difficult are occlusions, like for instance like a  
[unintelligible] - excuse me, a [unintelligible]  
category two level has density, unilateral density,  
and there might be something else behind it. And  
radiologists find it very hard because you generally  
only have two viewpoints, and it's very hard to make  
out what is [unintelligible] tissue. My question is  
does the 3-D tomo image help in that?

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01:10:50 ANDREW MAIDMENT: Right. So, there's sort of two advantages that the tomosynthesis can give. One is the example that I showed so that there's this sort of matting [ph.] that obscures the tissue. And so that improves your sensitivity. You are going to find more cancers. But yes, you could have an improvement in specificity as well. So, it's fairly common to see, you know, there's some glandular tissue at one plane in the breast, there's some glandular tissue at the other plane in the breast that when it's superimposed in one two-dimensional view, you see something that looks very suspicious.

01:11:21 It has the hallmarks of spiculated appearance. Now, in the second view you don't see that, right. And so we don't call that a mass; we call that a density because it's not - it's substantiated in both views. All right. But there are times when you don't see cancers in both views. So, we typically have to pursue that. And so I think part of the reason you're seeing a reduction in callback rate is that we're able to discern these sort of false lesions because they are not substantiated in three dimensions because they're separated.

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01:11:53 And so we're seeing both effects. We're seeing an increase in sensitivity and increase in the specificity. The interesting thing that wasn't shown, and I didn't have the - I had to choose which graphs to show, and that was a Rafferty study. They had to actually do this study twice because what they found was that the radiologist in the first [unintelligible] tremendously improved their - reduced their callback rate.

01:12:16 So, they went from callback rates of say 8 to 10 percent down to 3, 4, 5 percent. And their cancer detection decreased ever so slightly. They dropped one or two subtle tumors. And so what they had to do was basically go back and then retrain the observers as to what you should be looking for. And the second time they did the study, a different group of observers now because they basically learned how to teach this subject, the recall rate didn't decrease as much, but the cancer rate never did really decrease. In fact it increased.

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01:12:48       And if you looked, basically you were still on the same ROC curve in both instances, but what you're talking about is changing your operating points. So, from an operating point with very high sensitivity to very high specificity. And then the second time sort of an intermediate point where you're doing sort of a still a high sensitivity to a slightly higher sensitivity, slightly higher specificity.

01:13:14       LYNNE PADGETT: One more question and then we'll [inaudible].

FEMALE: So, I had a question of clarification. At the end of your talk you showed a series of displays and ended by summarizing what we thought was a tumor was the whole breast. I didn't quite understand. I thought those were...

ANDREW MAIDMENT: So, in this...

FEMALE: What are we looking at?

01:13:32       ANDREW MAIDMENT: ...particular instance - I'm sure we can get the mouse up here. If I can't - there it is. See, there's a surgical clip right there, a little bright white object, and there's a little round mass. And so that's what the radiologist

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detected. It detected that little object. And they put a clip in - they put a needle into it to do a biopsy, identified that it had cancerous tissue, put a surgical clip in there to guide the surgeon when an [unintelligible] was being done - would be done.

01:14:00 But in the interim this patient went for an MRI. And so we tagged on this contrast-enhanced tomosynthesis study at the same time. The result of the MRI and the contrast-enhanced tomosynthesis study is that there's a sort of - where'd the mouse go? There's a sort of broad area of enhancement, that this glandular tissue was picking up contrast agent that really it shouldn't have been doing. It should not be that metabolically active.

01:14:24 And it turned out that this woman's entire breast basically was full of cancer. And so she ended up having to have a full mastectomy rather than sort of a more conservative surgical option. And things like this are what are able to influence the survival rate in breast cancer because you have this ability to sort of - we would have missed, you know, the majority of her cancer, had her gone home, and then

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three months later come back with like an enormous tumor and very likely, you know, something that would end up shortening her life. [applause]

01:16:03 MALE: Oh, we have something, something that - what happened?

01:16:33 EDWARD VUL: Okay. I followed Todd's instructions to the T. I have one slide, no animations. Here it all is right in front of you. All right. So, what my lab does is we're largely interested in how people extract - using structured statistical models to characterize how people extract irregularities in the world and then exploit them to guide their behavior and perhaps their perception sometimes.

01:17:00 And so then I was trying to figure out how this all relates to medical imaging. And it all relates to medical imaging really via one paper from 1962 by Tuddenham who talked about how radiologists really what they're looking for is will they stop and many errors arise when they have satisfied the search for [unintelligible]. So, satisfaction of search is

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something that people have studied a lot, which is essentially a portion of what Tuddenham described.

01:17:25 What he described as satisfaction of search is that if you take a radiological image and you insert a fake lesion into it, people are less likely to find the real lesion that was there because they found the fake one and they're content, they were satisfied in their search and they moved on. So, this kind of behavior we can study in terms of the - well, we can look to see whether this kind of learning of statistical structure influences this kind of behavior.

01:17:49 So, I can't move from here. I don't have a mic. I'm going to point this at myself over here. Okay. Good. Okay. So, what we did - okay. Use the mic, the mic [unintelligible]. I don't get the point. All right. Use the mouse? Okay. All right. Here's the mouse. Nope. Oh, no. Oh, see this is what happens when you [unintelligible] mouse. This is all a trick. All right. Is this a laser pointer or is this a lightsaber? Okay.



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01:18:21 So, [unintelligible] will do is they learned they were searching for targets in a bunch of display, and we wanted to see to what extent they can extract this [unintelligible] in these displays. So, we had some displays contain many targets and some displays contain few targets. The expected number of targets was constant. So, it wasn't like a rarity kind of search. But we essentially had the displays clustered. So, in the 25 percent group lots of displays containing no targets and many displays contained a very large number of targets. In the 75 percent group few displays contained no targets, most displays contained one target, and a few contained a small number.

01:18:54 And so the question is to what extent does learning the statistical structure of the displays and how many of them tend to contain targets or not, does that drive behavior and does that dampen the extent to which you both have this satisfaction of search after they find the first target? So, the time it takes for people to start to quit searching is very much influenced by this structure. So, if they're in a situation where 25 percent of displays contain

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targets but they tend to contain many, when they find one target, they don't stop searching and they keep searching for a while even when they find two, three, or four.

01:19:24 In contrast if they're in displays where 75 percent of targets contain a target and, therefore, most of these displays contain few targets, they tend to stop searching early. So, by learning the clustering structure of the environment, people seem to drive the - the clustering structure of the environment of the [unintelligible] seems to drive their behavior and their strategy for searching over many displays.

01:19:44 The same kind of process - this is about satisfaction of search in general, of statistics and the structure of the environment drives satisfaction of search. But Tuddenham also noticed that it's the satisfaction of search for meaning rather than just search for a single target. And to get it back we have to talk about what does it mean to do the search for meaning. One kind of, one notion of this comes up in geospatial analysis where they call what they call sense making for geospatial analysts. And what

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they're looking for is really trying to make sense of an image and trying to search for explanations for what is really going on.

01:20:16 So, this is an example of Tuddenham's example of satisfaction of search. By virtue of finding something here people miss that. These pictures are examples of what he calls satisfaction of search for meaning. By virtue of knowing that there used to be some kind of tuberculosis stuff going on in the lung over here, and the second you look at that image a little bit later explains away or basically by knowing to look for the structure that was the tuberculosis, a new lesion that's somewhere in there that I can't spot because I'm not trained to do that, was missed by the radiologist because it was explained away by virtue of having found the structure before.

01:20:51 So, we can try to characterize that people look for structure in spatial displays and to try to characterize the finding of structure and, therefore, the explaining away that will happen. So, a very simple example of this is to look to see how people

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encode the positions of objects. All this is is really us trying to characterize the structures that people are looking for and how they drive their behavior. So, we can show people displays that are - or things that are clustered in various ways and then we can try to figure out to what extent do they represent these images by inspecting [ph.] the statistical structure and space.

01:21:21 So, the easiest way to show that they are inspecting these images is to look for the correlation in errors when they report all of these positions [ph.]. If they report all of these positions [ph.], we can see that in the case where there are four objects that are clustered into two clusters of two, two objects that are in the same cluster tend to have very highly correlated errors that are going to be displaced [ph.] in the same direction. When there's two clusters of four, the clustering structure of errors follows the clustering structure of the display.

01:21:44 When there's four clusters of two, the clustering structure follows those clusters or the error patterns follow the clustering structure of the

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display. So, basically people represent these images by encoding, by extracting the latent clustering structure and then coding what's going on with respect to the clustering structure. And this kind of process I imagine drives at least some of the satisfaction of the search for meaning which Tuddenham talked about, which is basically once you've extracted some kind of structure and you can explain away various anomalies with it, you tend to omit [ph.] alternative explanations for them, which are the second kind of pathology that might be in a given image. Okay. That's what I have. [applause]

01:22:26 EDWARD VUL: Yeah?

MALE: Is the clustering because there's no [unintelligible] generated model that constrains the spatial - there's no spatial constraint, it could be anywhere? So...

01:22:39 EDWARD VUL: Yeah. So, like why did the clusters [unintelligible]. So, we've done more things, and it's not always clusters. We can have slightly more complicated experiments with this iterated learning, and you can extract not just clusters; people also

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tend to extract lines and contours, which is like the same stuff that [unintelligible] talked a while ago and we can then statistically characterize the properties of these sorts of structures. But if we are looking at an actual radiology image, the structure is going to be much more than just spatial [unintelligible] together because the actual structures that exist in a radiology image are much more structured than that, and presumably the people are going to be explaining things away in light of those structures. Yeah?

01:23:16 MALE: Yeah. Is satisfaction of search reduced if the second target was from the same category as the first target?

01:23:26 EDWARD VUL: Satisfaction of search reduced if the second target is from the same category as the first target? I don't know. Jeremy probably knows.

01:23:36 MALE: I'm not sure if that's been directly done. And there are experiments that look at where the second target is. One of the famous satisfaction of search ones is where you're looking for a lung and

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they're removed a clavicle and then there are these ones where you're looking for two different tumors, but I'm not sure.

MALE: Miguel [ph.] is sure.

01:24:07

MALE: I'm remembering that [unintelligible] has given both - seen both examples given.

[unintelligible] multiple target and you find the first one and you give up and then the other one is like you say like these things that you're not looking for just like a bone fracture. I think that's one that - I don't know if it's [unintelligible] typically has shown where you're looking for some tumor and then there's a bone fracture that's so obvious and you...

MALE: That's a great example.

01:24:33

MALE: I think that's why they - I think - if I remember. Maybe Greg can remember. I think he chose that one.

MALE: Yeah. He's going to [inaudible].

MALE: Both - both...

MALE: I don't think he compares whether it's reduced or not in those two cases.

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[crosstalk]

01:24:47 MALE: ...comparison of which one [unintelligible].  
Yeah. And that would be sort of hard to because they  
would be [unintelligible] by the visibility of each  
of them [unintelligible].  
MALE: Getting back to our implied question of  
earlier about whether the viewing of different  
pathology should be [unintelligible] or not.

01:25:02 MALE: Yeah. Yeah. It would be hard to equate the  
two conditions. There's also a question in some of  
these things about whether you're looking at what you  
would really want to call satisfaction of search  
versus in effect a kind of probability summation. If  
you've got an 80 percent chance of finding one  
target, it's not a huge surprise to discover that  
you've got a 64 percent chance of finding both of the  
targets. And there are a number of satisfaction of  
search papers where it looks like the failure to find  
the second target could be explained simply by the  
fact that of course you're going to be less likely to  
find the second target under those sort of  
circumstances.



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01:25:41 MALE: But then that's not the case. That doesn't  
explain all satisfaction...  
MALE: Oh, no, no. By all means. Okay. Right.  
[unintelligible]  
MALE: There are many things under the satisfaction  
of search.  
MALE: Right.  
MALE: And where's Kevin? Kevin Burbound [ph.] is  
the satisfaction of search god.

01:26:00 MALE: I invited him, but he didn't come.  
MALE: [inaudible] listening to this on the webinar.  
[laughter]  
MALE: Could I make one other point? It's that a  
radiologist oftentimes has additional considerations  
that are oftentimes not really captured in these  
[inaudible].  
MALE: Yeah.  
MALE: For example, if you're going to go do a  
follow-up study that's going to involve some sort of  
whole-body CT or something like that, as long as you  
detect something, they're going to find whatever else  
is there. So, they don't need to...

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01:26:29 MALE: They don't actually find all the targets.  
MALE: [inaudible] find one and in some cases that's  
just as good as finding everything. So, you have  
to...  
MALE: Because somebody else is going to be doing a  
more thorough search.  
MALE: The next step is going to find the rest of the  
stuff. So, you...  
MALE: But the next step, aren't they also going to  
have to search for multiple targets?  
MALE: Yeah, but it's going to be a much more  
powerful exam. So, they're going to have a much  
better stimulus on which to perform that search. So,  
you have to be aware that [inaudible]...  
MALE: There's no - the incentives are not aligned to  
find one [inaudible]...  
01:26:59 MALE: ...what you make radiologists do. And some of  
these things are extremely low prevalence. The  
missing clavicle, if you're going to make  
radiologists report on the clavicle status of every  
patient they see, they're going to get kind of mad at

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you. So, a lot of those things are extremely low prevalence.

MALE: Right.

MALE: And you get to the case where we tend not to detect things that are low prevalent.

MALE: Yeah. That makes sense.

01:27:22 MALE: This is my question about computer-aided diagnosis. And there's been a lot of work about which I know nothing on modeling or using sort of a human psychology to drive more efficient methods to make computers do stuff. So, I guess my question is is any of this adaptive or maladaptive and useful for designing how computers might go about this problem?

01:27:51 EDWARD VUL: I think it could be used to adapt a computer-assisted display. So, if you know what the structure is of what structure people are going to infer from an image or if you can approximate it, then you can try to figure out which features of the image are going to be obscured to the observer and then accentuate them. So, there's the kind of thing that we've tried to do for geospatial analysts in the NGO - not the NGO, the NGA.

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01:28:21       And basically the idea is to figure out what kinds of features in a satellite image or a [unintelligible] or in a radiogram are going to jump out and are going to get clustered together, are going to form a structure and therefore and will be explained away by virtue of their clustering and perhaps then you can highlight deviations from what might happen. So, I think it's possible. I don't know to what extent it would succeed, but I think there's certainly room for something like that to happen.

01:28:47       MALE: And I guess satisfaction, search satisfaction is an accommodation to the fact that we're flesh and blood and get tired and have other things to do, but computers don't presumably.

EDWARD VUL: Right.

MALE: Or at least if there's sufficient power and bandwidth.

EDWARD VUL: Right.

MALE: So, this doesn't map [ph.] the computer-based...?

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01:29:07 MALE: No. But so the question is can you, knowing what kinds of errors radiologists might make, can you design a computer system to compensate for them and to help them? You certainly don't want to emulate a computer system to produce the same kinds of errors that people do. That wouldn't be very productive. But if you know what kinds of errors you're trying to anticipate and avoid, you can then perhaps design something to circumvent them.

01:29:29 MALE: [unintelligible] area many computer applications for medical image detection problems are kind of designed to be spellcheckers to kind of overcome satisfaction of search or fatigue or speed, and at least that's how a lot of these devices started out, especially on the mammography side. But then there's other computer applications that are trying to be more than what a spellchecker would be.

01:30:08 MALE: Does this not work?  
[crosstalk]

01:30:13 FEMALE: So, I guess does this mean that if the computer detects a bunch of things and shows it to

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the radiologist and gives them context [ph.] and says  
all these things could be wrong, then it will improve  
the radiologist?

01:30:31 EDWARD VUL: If you present them in isolation  
perhaps.

FEMALE: Yeah. They would start - yeah.

[inaudible response from audience]

EDWARD VUL: Oh, if you just have a very low  
threshold for a computer system for - to detect  
everything, that would be [inaudible].

FEMALE: I mean [unintelligible] satisfaction going  
on, right. So, if you tell them this is something  
anybody can pick out so don't look at this, look at  
something else, then that would mean that it would  
improve. If you say eliminate all this, don't look  
at it, this is the first thing you would look for,  
and you'll get satisfied. Start looking for  
something more difficult.

01:31:04 EDWARD VUL: Well, I think you don't want to miss the  
obvious one either by hiding it from the radiologist.  
Insofar as you have a system that successfully  
detects something that - or detects something that a

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radiologist should look at, you can perhaps present it to them after they're done inspecting the image on their own if they may have missed it, but you're certainly not going to want to present them with boatloads of false alarms because that would be a huge pain in the ass for the radiologist I imagine.  
[unintelligible]

01:31:34 So, I think a fairly high threshold for such an automated detection system, combined with presenting an after-the-fact after the radiologist did their own screening might help.

01:31:45 FEMALE: We do a lot of lesion detection. So, in that case what they prefer, at least the radiologists I work with, is that you show them the lesion. They would prefer to go in and [unintelligible]. So, it would be increasing the size or decreasing the size, but they would like to know where the context [ph.] is. So, that's what I was saying.

01:32:07 EDWARD VUL: So, in that case the computer vision algorithm can detect the lesion pretty well without needing intervention from the radiologist.

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FEMALE: It can, but there are a lot of false positives. The question is you can spend a lot of your time trying to get rid of false positives in a classifier or you can bring in the human [unintelligible] and say look here, here, here, here and then correct it, which is easier for a human than to train the computer to do that.

01:32:34 MALE: I was just going to ask a question that Miguel asked me actually, which is just showing very powerfully that people are sensitive to the distribution of the number of targets and to the spatial locations of objects. How much of this is task-dependent? So, presumably you learn about the number of targets by doing visual search.

01:32:53 MALE: So, in this case we train them on the number of targets and we try to push them around by training them on different distribution of targets.

01:32:57 MALE: Well, I'm wondering to what extent if people extract regularities very robustly and in an experience-dependent way, could you make people better at doing search or spatial localization or



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whatever the ultimate task is just simply by exposure to stimuli, just learning, just incidental learning of the spatial structure of these medical images?

01:33:23 EDWARD VUL: I mean so Jeremy probably knows a lot more about this because he's tried to insert guns into TSA bags or something like that. But I think by virtue of increasing the prevalence and changing the distribution of targets that screeners see change their criteria. Right, Jeremy?

01:33:38 MALE: Well, actually the more the relevant data point for what Nick's talking about might be the old eye tracking data from the Kundel and Nodine establishment and Elizabeth Krupinski actually and elsewhere - who is listening now. Hi, Elizabeth. That shows that one of the main effects of becoming an expert in a domain like radiology is cutting way down on the number of eye movements you make because in effect you learn the structure and you use that structure to say there's just not going to be anything there.

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01:34:14 MALE: Yeah. I was thinking of something very similar, and I should probably know this. But what is the relationship between a satisfaction of search and eye position? So, is it the case that when you do have satisfaction of search, you simply don't look in the mammography where the other target is or do you change your decision criteria, you look there but you [inaudible] the target?

01:34:36 MALE: You definitely tend to stop earlier, and I don't know if your criterion [unintelligible] on your fixation to landing on the second has changed.

01:34:44 MALE: So, you definitely stop earlier sometimes. And Kevin Burbound has data where you can show that it's not just that you stopped early. And again, if you go with the eye movement data, the sort of classic again Kundel/Nodine - hi, Elizabeth - Krupinski kind of data tends to break errors into three different varieties. There were search errors where you don't ever fixate on the item. There are - I can't remember the terminology.

MALE: Perceptual.

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01:35:18 MALE: Perceptual errors where you fixated on it but you didn't hang around long enough to think about it, that you clearly got your fixation on it. And then there are decision errors where you stared at it and just called it wrong. And sort of classically figure about one-third each for those type of errors. So, the important point for what you were asking about is that it is not the case that missed errors in this domain are just because you didn't look at it. There are lots of [inaudible] look at it and then...

01:35:51 MALE: Does the distribution of those three kinds of errors change in satisfaction of search with the second target or does that level - is that granularity of analysis not something that we know? You're saying it's one-third [unintelligible] altogether, but what about the second target?

01:36:07 MALE: And even if it is just one-third, after one-third - that's one-third of the errors that would be [inaudible]...

MALE: Oh, yeah. And so we've been looking at the situation where you're not looking at a single 2-D image, but you're looking through a stack of images.

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And we think that the proportion of search errors is going up as the - as you move from these 2-D frames to a 3-D volume of data because people don't really know where they've looked.

01:36:41 MALE: It's worth also noting that Steve Michoff [ph.] claims that satisfaction of search is not - is in some cases a byproduct of an intentional blink, which is when you have two targets in quick succession, you're essentially still processing the first target and so you may look directly at the second target, but it's sort of gated [ph.] out of processing. So, he's got evidence that that at least will happen in like those stimuli in the upper left corner there.

01:37:10 LYNNE PADGETT: Okay. I'm going to step in [inaudible] So, this is not really a valued potential skill, but it is valuable [unintelligible]. So, I would like for all of you to go enjoy about 12 minutes of your break and then about three minutes 'til 11 [unintelligible] experience a mild level of anxiety that is only relieved by [inaudible]. I'm done. And I will turn it over to Kristin.

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01:37:52 [BREAK]

01:53:31 [BREAK ENDS]

01:53:40 BRANDON GALLAS: Am I given the clear to go? Is that  
what you do?

KRISTIN LITZELMAN: Yeah. [inaudible] just want to  
[inaudible]...

BRANDON GALLAS: Excuse me. Excuse me.

KRISTIN LITZELMAN: We're going to [inaudible]. So,  
with that, Brandon, go ahead.

01:54:07 BRANDON GALLAS: So, I want to express one thing  
because I don't want to do it to each speaker as we  
go. I kind of nailed someone early, but when I'm  
sitting in the audience, I'm always wondering about  
how does your research impact me in imaging  
evaluation and the product that comes through the  
FDA?

01:54:28 So, maybe that won't come up all the time here, but I  
think a lot of the vision scientist researchers, if  
there was definitely an effort to partner with your  
clinical colleague that you probably may or may not

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speaking to at all yet, I think to understand them, to walk through their day sometimes and see their workflows, to inspire better and more targeted experiments would be hugely impactful in making the leap from vision science to impacting medical image quality.

01:55:05 And whether or not you actually use medical images in your studies, obviously when it gets received by clinicians, if it doesn't have medical images and they kind of - their eyes glaze over. So, when the studies have medical images, you get a lot more impact from the medical imaging community and a lot of translation. I can sell vision science ideas to my upper management if the studies have actually been done with medical images.

01:55:34 But of course it's just the challenge that you're seeing in the workflow and the technology. You motivate your studies much more tightly than maybe and you only have access to teddy bears or mountains and things like that. I understand all that and where we live and who we actually have the ability to relate with.

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01:55:55 But I just want to make that point really clear because if vision science is really to impact medical imaging, that groundwork in understanding those workflows - and someone said does something depend on the task. It always depends on the task. There's no imaging question or vision science question that doesn't depend on the task, that doesn't depend on the images, that doesn't depend on the features in the images. So, I just wanted to give that little speech up front.

01:56:29 I used some previous slides, cut them down just to try and fit the goal of this meeting. So, this was more of an introduction of me earlier, but then kind of whitewashed it to be about our group. [unintelligible] is the leader of our group. And some of the things that happen in our group. This is the Division of Imaging and Diagnostics and Software Reliability within the research arm of the Center for Devices and Radiological Help.

01:56:58 And so we see imaging devices and we try and provide the consultation on what the sponsors bring to us.

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We review what they bring to us and provide the expertise on some of these parts of the technology, whether it's the physics - there's a lot of people in our group who are experts in the physics of medical imaging, x-rays and ultrasound and MRI.

01:57:19 I mostly play a role in evaluating clinical trials, the study designs and the analysis method behind them, and especially trying to always raise the flag of reader variability. I think radiology has embraced the idea of reader variability. And there's a great article by the editors of the *Journal of Radiology* where they really say that we need to understand reader variability. It's not enough to do a study with one, two, or three readers. We need to have studies that really explore and characterize reader variability.

01:57:53 Mammography is one of the most studied imaging modalities in the medical imaging field. So, a lot of test cases and examples and a lot of our experiences come from that field. And then computer aids is where me and my colleagues spend also a lot of - and that's the diagnostics of our division where



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you take measurements and a computer tries to help the clinician, whether it's a magic score or whether it's prompts pointing at features in the image and those sorts of things.

01:58:23 And recently I've been spending a lot of time in digital pathology because it is going through what mammography went through in the early part of this new century. Mammography went digital, and pathology is trying to go digital. Digital pathology kind of embraces all the information of the patient. The actual technology is referred as whole-slide imaging, and that's where you take a slide and you give it to a scanner and it creates a digital image, and there's a lot of exciting things happening there.

01:58:51 But like I said, these are really where I'm working right now and spending a lot of my efforts. And one of the things we're really trying to do is to create resources. I think more and more we understand that having the end-user tools available for investigators and manufacturers really helps to convey what we write in our little scientific papers that [unintelligible] people can understand. To actually

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turn that into a tool that is available to the end-users is really what we recognize as a way to disseminate that.

01:59:22 And Chicago and Iowa have been real leaders on the reader variability and the evaluation of performance in medical studies, in medical imaging studies. So, we have a page that kind of tries to - that is in that space as well and trying to simulate, analyze size and power reader studies for different kinds of endpoints.

01:59:46 In the digital pathology world I've been working on a platform to evaluate digital pathology as compared to optimal [unintelligible]. And this software, the key to this software is that it registers the glass slide that's on the microscope to the digital rescanned image that was done by the scanner so that you can have a pathologist look at very specific regions or very specific cells down to the cell level in their evaluation. And they go through all these lists of regions or cells in both modes so that you can get really tightly correlated observations in both of those modalities.

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02:00:24 And then lastly I've been building a working group in this space to try and take some of the things that we know about reader studies in general, the analysis and the sizing and the methods related to running studies and study designs to the community. Pathology is really great at QA and QC over time. They build in that failsafe. But in terms of technology evaluation, they haven't been in that space a long time because the microscope has been around since the previous century, 1900s is when that came in.

02:00:58 So, it really hasn't gone through technology evaluation that we need to see to get digital pathology in the hands of everybody. So, I think that's what I came to share. [applause]

02:01:18 MALE: Can you say a little word about that top code on the right? That iMRMC thing, what's that do?

02:01:26 BRANDON GALLAS: So, in radiology and mammography especially, evaluating CT systems or CAT systems that have the reader as part of the technology. It's hard

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to evaluate a technology without the reader when you're talking about imaging because it's all about what task is trying to be done with the image. That's the whole point we take the image is to do something with it.

02:01:51 And so radiology has a pretty good history of doing ROC studies where you have a set of cases and you have a group of readers and you have all the readers read the cases. And for a task, a binary task is what ROC analysis is good for. Obviously generalizing that to other kinds of tasks gets more complicated. But if we can reduce it down to a binary cancer - no cancer, a tumor exists or doesn't exist, this is inflammation, this is not inflammation, that's what ROC experiment is good for.

02:02:25 So, these packages can take data from an ROC study like that and do the uncertainty analysis and the hypothesis testing of that study to compare to a modality, either the standard practice in the new technology or to do just the technology by itself. And so that's what the software does. It takes the reader study data and gives you the estimates of

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performance as measured by AEC [ph.]. And sensitivity and specificity or other metrics, we're always trying to generalize the endpoints that you can do with these software packages.

02:03:04 Right now it's geared towards ROC and sensitivity and specificity or binary performance metrics. And so the other piece to the simulation part is where we simulate these kind of reader studies where we include all those random effects, not all of them, but the key random effect that we think really pushed the needle in terms of uncertainty, and that being variability from the cases, the patients, and the variability from that human reader and the fact that each reader - you can't get three readers to agree on anything when you're talking about a lot of these studies unless it's the most trivial of tasks.

02:03:41 If it's a trivial task, then there's agreement. But the challenging task is where we're trying to always measure things. And so there's a lot of disagreement and reader variability. So, these error bars, they account for a study that has new readers and new cases. And that's - we simulate those kind of

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studies and we analyze those kind of studies. And then we have always the biggest question when I collaborate with people or people reach out to me is well, how big do I need my study to be because that's where the money comes in and how much you have to pay readers or how much it costs to select cases.

02:04:13

And so we have made good progress on sizing studies in the community as tools [unintelligible] the Iowa software and the Chicago software are all great resources for doing that. So, anyone who doesn't account for reader variability, I think they are either in the early phase of their studies, which is fine. Everybody starts somewhere and they only have one reader for this study and three readers for this study.

02:04:38

But when we start getting towards coming to the FDA, you need to account for reader variability, and those studies need to capture the variability and account for it in the [unintelligible].

02:04:54

MALE: I'm going to ask a blissfully ignorant question if that's okay. My lab does MRI, functional

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MRI. About half of our work is functional MRI. And I would be laughed out of the room if we had human observers reading fMRI images. And this idea of human readers doesn't exist in the "medical imaging community" within, you know, cognitive neuroscience. And so I understand there's a long history here.

02:05:24

And obviously there's human expertise that can be brought to bear, but everything we do, we're trying to detect, you know, one percent signal changes in the images. Everything we're doing is with statistical models of various levels of sophistication. And so this is more of a general question. It's a naïve question I'm sure. But what is the critical role of readers and in the future can you not imagine a sophisticated statistical model that can get away from the need to have readers who deal with that kind of variability that you're talking about?

02:06:00

BRANDON GALLAS: So, every task is different. And the regime that you're working in is basic research. And so I said one reader or three readers is where a lot of technology start out with imaging, but yours

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is in an imaging modality that doesn't have a way for us to look at the images.

MALE: Exactly.

BRANDON GALLAS: Three-D images are tough. You can't look at a mass spect image or hyperspectral imaging just by getting the data.

MALE: Right.

02:06:26

BRANDON GALLAS: So, if the technology that you're working on translates into an image that will be given to a reader for interpretation, then that's when you start having the need to demonstrate that it's useful to readers. And that technology development then starts with one or two of the collaborators that are in the development process to when you really want to start selling this device or this process. That's when you have to come to the FDA.

02:06:55

MALE: And another piece of this is that the questions that you're asking are fundamentally different than clinical questions, and nobody will actually take you to court if you miss a main effect. Whereas, if you...



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MALE: [inaudible] variability, you know.

MALE: Well, yeah. So, computer systems in something like mammo - Brandon is in a much better position to get this right than I am, but my understanding is the computer systems in mammo are about as good as a good radiologist, which means that they still miss some cancers.

02:07:37 And if you were to say well, it's just about as good as a human and we could just run it off of the computer, somebody's going to get their pants sued off in ways that would not happen in cognitive neuroscience.

02:07:54 MALE: Well, they're not quite to the level of a human reader or people would be trying to sell it that way or be trying to demonstrate it. So, right now the best way for [unintelligible] is with the human as part of that effort.

02:08:08 MALE: I think there's another difference in that you're looking for median signal changes, which are easy to look for statistically; whereas, the signature of a lesion or a tumor is a particular

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shape density combination. So like if you're looking for - in marine biology they try to classify algae, and it seems like a simple computer vision problem, but it's a huge pain in the ass because what defines an algae is the particular branching structure of it, and that's hard. That kind of structure that you're looking for that a human can [unintelligible] recognize, it's much harder to get a computer to recognize.

02:08:39 Whereas, to recognize its difference in signals, strengths or just brightness over a bunch of samples, that's much easier. So, I think it's a little different in terms of what you're looking for, and computer vision [unintelligible] ends up harder.

02:08:54 FEMALE: I wanted to comment, yeah, because I'm working on [unintelligible]. So, I've been working on whole-slide imaging for more than 15 years [unintelligible]. So then say like now the [unintelligible] many people think whole-slide imaging have the information, can make the diagnosis, but it's not [unintelligible] and now go back into

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even the [unintelligible] is also important and how  
to fix it.

02:09:32 So, we tried to automate everything. So, like not  
only the whole slide [unintelligible] to improve  
whole-slide image, we had to go back  
[unintelligible].

02:09:54 FEMALE: We have a comment from Russell Hammer [ph.]  
who is saying in mammography unlike fMRI you need to  
be doing sophisticated pattern detection or  
identification. So, it is for now essential to take  
advantage of this [unintelligible] patterns  
[unintelligible] mechanism.

02:10:16 BRANDON GALLAS: Just to respond to that very  
briefly, we are developing very sophisticated machine  
learning methods for pattern recognition in fMRI  
data. So, in principle you could do the same thing.  
It may not work as well. That's outside my domain.

02:10:28 MALE: You just have to get FDA approval.

MALE: If you want to sell it. [laughter] If you  
don't want to - I mean that came up earlier. If

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you're working tightly in a specific place and you're doing research, that's not an FDA issue. It's when you want to sell your product.

02:10:49 MALE: So, I just want to make sure people understand the magnitude of these studies. The iMRMC, the multi-reader, multi-case study. So, on the tomosynthesis device Andrew's talking about the reader study costs more than \$1 million, millions of dollars to do that reader study to collect the cases, to get the readers who are radiologists, trained radiologists, to bring them out, train them well enough and get them to do it, and you're protecting a several hundred million dollar investment of technology development in the device. So, this is not small-scale stuff. A lot of people have a lot riding on [inaudible].

02:11:25 MALE: Right. I mean the reason we developed the [unintelligible] platform was in working with Barco, you know, they had examples where they thought certain innovations were going to improve things and they did not. And the cost to create an LCD monitor from idea to two years in clinic with proof is about

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\$100 million. [unintelligible] spent over \$500 million to get to the point where they could go to CMS and try to get a code for tomosynthesis. These are enormous investments, and they're not coming back in terms of the sales costs or the technology or anything else.

02:12:02 KRISTIN LITZELMAN: I'm going to [inaudible].  
[applause]

02:12:39 CATHLEEN MOORE: I should have closed my email.  
Don't look at my email. Sorry, guys. Really, it's in there somewhere.

MALE: Are you going to [inaudible]?

CATHLEEN MOORE: I was emailing over the break.  
Okay. Here it is.

02:13:10 Okay. So, what I'm going to talk about is not ready to go to the FDA. So, I do basic work on perception. And I'm actually at Iowa, though shockingly I haven't interacted with [unintelligible]. If they're listening, tell them we really need to get together. I haven't worked in medical imaging at all, though I have done some work indirectly through students on

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life guarding, surveillance in life guarding, which actually presents some similar issues in terms of ill-defined targets and the need for human viewers.

02:13:47 So, I'm going to tell you about - I don't have one slide. I did not accept the challenge. So, I have a bunch of movies and demos, and I'm not going to try to present a lot of data. What I want to try to do is convey some of the ideas that we think about and how they might be relevant to medical imaging issues and then just tell you a little bit of what we've done in the lab by way of nutshell summaries and demos. And those of you that want data and papers, I'm happy to talk to you afterwards.

02:14:16 Okay. So, we all know about perceptual organization, grouping similar things together; completing surfaces behind or [unintelligible] surfaces or in front of; segregating different parts of the images into units, figure and ground for example; continuation and closure. And a lot of the work, the basic work in perceptual organization has been concerned with identifying the rules by which these things unfold.

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How do we take a raw image and parse it up into its relevant unit?

02:14:43      And I think of that as the form of perceptual organization. One of the things that we've been trying to think about in our lab is well, that's fine, but what is it that perceptual organization does? What is the function of it? What are the consequences of it in terms of visual processing and visual perception? And an overarching view that we hold is that perceptual organization guides the dynamic updating of visual representation by defining temporary channels.

02:15:11      So, the idea is that vision is a process. And to the extent that your eyes are open and there's lights on in the room, we're continuously sampling more information. So, we somehow have to integrate incoming information with the existing representations that we have. And our idea is that perceptual organization essentially defines the channels by which that information is guided and used to represent the information that's coming in.

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02:15:38       What does that mean? What's the implication of that?  
Well, organization processes essentially set the  
stage for what information can be represented. And  
that means that if the fundamental organization that  
the system adopts, the way it interprets the raw  
image in terms of the relevant functional potential,  
functional unit, then the information may be  
unavailable. And I have "wrong" in quotes here  
because the visual system can't be wrong. It's the  
way it makes sense out of the scene.

02:16:06       But depending on the task and depending on the  
information that you're trying to extract such as  
interpreting medical images, if you start off with  
the fundamentally wrong organization, then you're not  
going to be able to recognize the meaning of the  
units. So, we see this, of course, nature taking  
advantage of this kind of thing. So, here's a  
camouflage. I don't know if you can see - I can't  
see it from this angle. There's a beastie in there.  
Can you find it? Have they found it? Thank you.  
[inaudible response from audience, laughter] Exactly.



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02:16:41 And here's another one. And the idea is sort of why does camouflage work and how are these things taken advantage of? Well, it's the way that the system is. It's not just about - I mean some of it of course is relevant to basic contrast issues, but that's not the only thing, right. It's that things have blended into the background and are no longer a unit. And if they're no longer a unit, then you don't try to categorize it or make sense out of it. There's a spider beastie in there.

02:17:11 And this is my favorite modern-day camouflage [unintelligible]. Okay. So, how is this relevant? Well, here's an image that I pulled off of the Virtual Med Student. Here's a pathology image of a glioblastoma patient. And you see this little note here, notice how the cells line up, da, da, da, da, da. Well, [unintelligible] know, I didn't notice that at all, and I would definitely need these particular arrows to indicate it.

02:17:39 And over time as I sort of sat and looked at my talk and thought about these slides, actually the organization of that has started to come out in ways

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that it wasn't when I first looked at it. I don't see any organization there, but over time you do. And in order to identify this kind of whatever's wrong in this slide, in this image, you need to have organized it properly, right. You need to know what are the relevant units and what's the organization of it.

02:18:06 So, here we have, again taken from the Virtual Med Student, a lot of imaging techniques, as I understand them, are aimed at highlighting or contrasting those things that are relevant to the particular issue that you're looking for, but you want to think about in doing that are you making the system blind to other things because by highlighting one organization you necessarily eliminate the possibility of other organizations.

02:18:31 This is related to the familiar hidden figure situation. So, where this is an old set of stimuli and tasks where you're looking for that particular shape there, that kind of arrowhead shape in the more complex one. And that's really hard to do. It's harder to do for some people than others. It's

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really hard for me despite the fact that I spend my  
life working on these kinds of things.

02:18:52      Once you find it - so here, that's where it is. But  
why is that so hard to find? It's not about the  
contrast of the edges, it's not about the quality of  
the visual image, but it's about the way that it gets  
integrated and organized into the broader context  
that you move it. You can't find it. You can't see  
it.

02:19:11      So, what do we do in our lab? We try to ask  
questions about how basic visual processes are  
mediated by the perceived organization of the scene.  
Okay. So, what are the consequences for things like  
basic visibility of an image of - sorry - what are  
the consequences for basic things like basic  
visibility of an image due to the way that we  
organize the scene?

02:19:37      And this is, again, this is just sort of a  
[unintelligible], this is an experiment that we had  
run, but it demonstrates things. So, here on these  
two different movies you have exactly the same timing

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of two separate stimuli [unintelligible]. I'm presenting a stimulus one after the other for I don't know, 30 milliseconds or so each, flashing it. And in one case you have it being perceived as a single object that's morphing over time.

02:20:01

And on that left-hand side you can perceive them as separate letters and in fact as you view it, you might even be able to see that they're spelling out some words. There's nothing different about the timing of the stimuli or [unintelligible] contrast, et cetera. And if I asked you to do something like, for example, identify the identity of the red letters, you could do that in the left-hand movie. If instead I asked you to identify the shape of the mouth in the right-hand image, you'd have a much harder time doing that.

02:20:30

Why is that? Well, in one case you're perceiving this as a changing single object. And so the consequence later, stimuli overweighed information about its earlier [unintelligible]. Whereas, in the other case it's protected, right, because they're separate objects. And yet [unintelligible]

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organization of these two different scenes have  
consequences for the way that we integrate later  
incoming information.

02:20:56 So, we'll stop. Okay. [unintelligible] I have more.  
I can go on and on. Sorry. All right. One last  
image. Did you just cut me off? No? Okay. So,  
here's a classic misperception of spatial location.  
So, this is a flash lag effect. In the movie on the  
left there the moving dot in the red...

02:21:19 [no audio]

02:22:06 CATHLEEN MOORE: Okay. Because this is just for the  
point of discussion. So, what are these kinds of  
things? So, I just want to point out that  
organization is fundamental to visual processing and  
that a given scene organization can render perfectly  
good information functionally invisible. And what  
we're looking for in imaging is looking for that  
important information, and if we've organized it  
differently, it can be gone. And what I didn't say  
is that attention to a great extent is also guided by

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the organization of the scene. And of course  
attention is quite relevant to these search tasks.

02:22:36 And then finally I want to emphasize that perception  
is a process and that organization determines the  
direction of that process. [applause]

02:22:48 [no audio]

02:23:09 MALE: The perceptual organization thing picks up  
very nicely on the tomosynthesis talk earlier because  
a lot of the problem with sort of classic 2-D mammo  
and other images is that you get these lovely  
perceptual structures that don't happen to actually  
reflect something that's going on underneath, but  
it's really hard to pull that out.

02:23:37 MALE: And there's sort of a flipside where there is  
structure there, but we can't see it, which I think  
is sort of what you're talking about. But this  
reminded me of some studies with newborns where  
different language groups have some sounds that  
people in that language group can very clearly hear  
and we can't, like tones in Chinese and clicks and

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that sort of thing. And it turns out that babies up to the age of 18 can hear all of these things, 18 months. [laughter] That's right.

02:24:08 And then by the time they've sort of heard enough of their language, they no longer can hear these other things. You can show by attentional reward. So, maybe infants are better at reading radiology images than we are.

02:24:27 MALE: Try to get that past the FDA. [laughter]

02:24:29 [no audio]

02:24:34 MALE: Or we could just start training them early, right. Enough of this Dr. Seuss stuff. Show them mammograms.

MALE: That's right. Find 3-D [inaudible].

02:24:47 MALE: I'll pick up on what Dr. Yagi commented on earlier, and that was all the issues related to the image quality, from preparing the sample correctly to the characteristics of the imaging device.

MALE: Sorry, you all. It's working now. One, two, three, four.

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MALE: I want to say that in radiology there is the early research that links what the readers are looking at to the characteristics of the imaging device, the noise characteristics, the correlations of objects within the image to understand how the human performance changes as you change the imaging characteristics.

02:25:30

So, I think when it comes to the imaging characteristics for pathology, that is a really needed enterprise to really build the understanding of the imaging characteristics, but then to understand how those characteristics can be degraded or improve and how those changes impact what people can accomplish, what they - their task performance.

02:25:55

And so that's a direction that our lab has a lot of history with in the radiology arena, and I think those kind of studies that link technical metrics to performance metrics on readers looking at images or image features, that's where there's a lot of opportunity for a lot of great study.



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02:26:20 MALE: Brandon, can you comment a little bit more on what are the perceptual challenges in visual pathology and how do they compare to something I'm more familiar with like x-ray imaging in terms of what are the limitations from a perceptual point of view [inaudible] very different, and I want to learn a little bit about what those - do you have any insights? It seems like it's a very different beast [ph.].

02:26:44 MALE: So, the biggest difference is that the pathologist's task is so diverse. Now, and that's the perceptual - I think that's where perception has the - I mean that's a huge challenge to try and deal with all those tasks that are in front of the pathologist for a single slide. And when I break it down for the technology evaluation, I am trying to narrow the task to one or two that the pathologist says well, that's not what I do; I do all these things.

02:27:17 But for the technology evaluation I want to make sure that the color is adequate, that the resolution is adequate. And when we have tasks that are so

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multifaceted, so many check boxes to do on a pathology checklist, that obscures the ability to understand whether this magnification or this resolution is actually impacting a more consolidated singular task.

02:27:47 And so that's why I mentioned that those kind of studies that really link the imaging characteristics to features might tell us a lot about the modality general across all the tasks that the pathologists are doing. So, if we can demonstrate that the level of color - people use the word fidelity. Color is big in fidelity. So, how much fidelity do you need to the actual what comes through on the microscope or what sort of resolution do you need to do this task at the [unintelligible] level or at the structural level or at whatever level? And so all that learning is really in front of us.

02:28:31 MALE: I'm going to be somewhat of a contrarian. I am a pathologist, and my basic sense is that the technology is the least of the problems and that the challenge is more pathologist training and the quality of the sample and the staining and everything

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upstream. And really we're dealing with good digital cameras, and they do a good job. And they're not the problem.

02:29:00 They're the thing that we can focus on and play with, but the problems are much more intractable like how good was the training, how good was the sample and/or workflow, attentional problems, ease of use of zooming and panning, and fatigue. And I think those are the real issues. It's workflow and usability rather than technical how many lines per inch and how many grayscale levels are you projecting. That would be my sort of hypothesis.

02:29:33 FEMALE: Yeah. [inaudible] but not the specific [unintelligible] that each machine [unintelligible] differences. So then they are using different equipment. In my presentation I have some slides...it depends on the sickness. And data-size is huge. So a 3-D model of a human brain it is 200 [unintelligible] for one brain [unintelligible]. That is huge.

02:30:17 So, right now we are thinking how we can receive huge data. But then also [unintelligible] more and more

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[unintelligible] they know what kind of image they like and what kind of colors they want to see and see a really useful image even if they don't need to make a diagnosis, but still they want to see it.

02:30:56 So, now [unintelligible] system more than like three years ago because now I see it as they want to see more - I mean higher. But I wonder what we have to do like do we have to decide [unintelligible].

02:31:20 MALE: That reminds me of what Henry - I think it was Henry Ford said when he asked what farmers wanted and they said we want faster horses. So, you don't want to listen to pathologists. [laughter] You want to analyze what actually goes on, and apparently if you look at trained versus untrained, the more time you spend at high power, the worse your diagnostic accuracy is. And the more time you spend - or the less time you spend and just use 4X, which is sort of the lowest usual power, the better you are, and that's the basis of training and confidence and experience.

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02:31:56       And so you can definitely get hung up on sort of  
resolution and contrast and color fidelity, but those  
may not be the most important things.

02:32:06       FEMALE: Yeah. So, the [unintelligible] when we're  
doing [unintelligible] using iPhone. So, that kind  
of image even they are satisfied [unintelligible]  
some opinions, but they [unintelligible] they have to  
use iPhone image for their regular basis.  
[unintelligible] that's why they don't compress [ph.]  
their data.

02:32:35       FEMALE: I have a question for I don't know who might  
be able to answer, but when people are being - what  
constitutes training in all of this? So, what are  
they being taught a because I think that's  
[inaudible].

02:32:47       MALE: Are you talking [inaudible] or radiology  
[inaudible]?

FEMALE: People who read medical images. So, both.  
Wait, so - like that's what - I mean when you're  
asking about relevance of perceptual research for  
these kinds of things, then I don't really know what

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people are being taught, and that could be  
[inaudible]. Yeah.

02:33:11 FEMALE: Yes. It's actually the preference of each  
pathologist, the color [ph.]. It depends on how they  
train, where [ph.] they train. Usually  
[unintelligible] microscope [ph.]. Many people  
looking at microscope, the same images. So, there's  
senior pathologist [unintelligible] explaining how to  
make a diagnosis, and the younger people just watch  
while asking some questions. So, that image  
[unintelligible]. So, then it depends on  
[unintelligible].

02:33:46 MALE: Like machine learning, it's train by example,  
and very often there's nothing verbal going on. They  
just say yeah, that looks like cancer [ph.]  
[unintelligible]. But it's amazingly tractable  
[ph.]. I have a high school student who basically  
just by sort of observing was able to then go into  
datasets and pull out the cancers in the normals and  
make me little slides of each.

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02:34:10 Of course, that's trivial in the sense that those are at the far end of the spectrum, and it's already an enriched dataset and it doesn't correlate with what real life is. But 90 percent of the time when the pathologist comes in with a stack of slides this deep, a lot of it is cancer. And so you have this expectation and you're attuned for it and you see it. But that doesn't answer your question.

02:34:35 FEMALE: [unintelligible].

MALE: When we've asked radiologists why you do X, it's often sort of a mentorship answer that this is the way that, you know, my senior taught me to do it. You look at the image in this order, you look at the image in this way. Plus they have excellent theories about exactly why this is the only possible way to do the task unconstrained by the fact process. But a lot of good theories out there.

02:35:09 MALE: [unintelligible] discussion, but can somebody remind me - I should know the answer to this, but I remember [unintelligible]. How do we establish [unintelligible]? [laughter] I know Brandon is - don't go there. It's a half hour, but...

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02:35:23 MALE: There's a good answer. Actually pathology is one of the best disciplines equipped to do this because there are sort of two developments. One is something called tissue microarrays, which is basically you can take lots of different chunks out of relevant regions and of many different cases and put them all on a single slide. So, you can look at 600 patients on one slide.

02:35:54 And secondly, we have 10, 20, 30-year follow-up and can say we called this cancer. Is it really cancer? Did they get it or not? And this is being very critically looked at. So, the ground truth is not what the pathologist says but what the patient did. And so in comparison to many fields, I think in theory we have really a good handle on that. Does that make sense?

02:36:18 MALE: Sure, it makes sense. I want to respond first that you did not have the contrarian opinion; you had the common opinion, and I had the contrarian opinion. And everyone should understand where I'm coming from. I'm coming from the FDA, and we're trying to have a



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method for evaluating these technologies that we can use over time to prove many of these.

02:36:45 And where do we want [unintelligible]? We want to use the technical measurements to say that this device should be on the market or not. And along the way that's where we want to be, but I don't think anyone's near that at this point. So, what is a current paradigm is to demonstrate that it is as effective. So, and that is demonstrated through doing studies with tasks using the new technology and maybe comparing it to the old technology.

02:37:14 And then when you think about that kind of study on the [unintelligible] topic as Miguel just brought up [unintelligible], there is no manufacturer in the world that's going to wait 20 or 30 years to do that. So, right now...

02:37:28 MALE: But these are retrospective. In other words, we have - that's the other thing, we can store patients in paraffin for 20 to 30 years.  
MALE: So, that is certainly on the table then and certainly is a viable reference method, and I'm happy

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to see it because that will give the statisticians a lot more comfort because the outcome is what it is. But the more common approach right now is certainly I think what I've seen in the literature is [unintelligible] the committee to determine the reference method [ph.].

02:38:04

And that committee is using the same modality as was used for the study. And so there's a kind of referencing the same modality to come up with the truth and any statistician will tell you that's illegal. But I think in terms of the [unintelligible] that we work with, that is a paradigm to be considered. And now how do you get this expert panel, and who is an expert are real big questions, and I think there are maybe directions to go alternative to the expert panel to say that the diagnosis by a group of your peers is also another idea for a reference method.

02:38:49

And so those are all the things that we're trying to investigate and understand what do you lose when you can't get an outcome as tight as having a 20-year follow-up, and how much do you lose when you can't

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find experts, and how much do you lose when you are using your peers as a reference method? So - or yourself as the reference method on the reference technologies, the optical microscope [unintelligible].

02:39:17 I think all that as part of the study design is what I'm saying should be worked out in these early studies that aren't as ambitious as trying to cover all [unintelligible] under the sun.

02:39:33 KRISTIN LITZELMAN: This is from [unintelligible] again for Cathleen actually. Do you have any ideas of how we might be able to optimize the organization of images so as to better promote the best perceptual organizational response so as to best extract the clinically relevant target features?

02:39:52 CATHLEEN MOORE: Yeah. So, that's - well, the short answer is no, I don't, but that's partly what was behind my question of how are people trained. In other words, what is it that they're looking for and how they're taught. So, I'm looking at [unintelligible] image and this is a tumor, this is a

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such and such like the slides that I was showing you from the online med student. Without the particular reference, I'd have no sense of what it is that I was looking at.

02:40:25 And my question was well okay, when you're training up people to do this, is there known explicit things that we're looking for or is it [unintelligible]? It sounds like it might be [unintelligible] in terms of just showing and watching and relative success. And if we can harness what is it that's being latched onto, then I think maybe that would point to how one might help optimize images to identify the relevant [inaudible] organization.

02:40:54 FEMALE: [unintelligible] try to make a diagnosis and then [unintelligible]. Also, [unintelligible] I mean [unintelligible] teaching and how many [unintelligible] how many [unintelligible] we have to count. So, that's one [unintelligible] easier to make it more like automated. [unintelligible] so these are some guidelines we have to look for [unintelligible].

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02:41:29 And also [unintelligible] the diagnosis between digital and glass slides are different. So, even like - we have [unintelligible] looking at the [unintelligible] images [unintelligible] images [unintelligible] microscope [unintelligible]. They have to discuss and[unintelligible].

02:42:02 In some of the study we did [unintelligible] diagnosis the microscope [unintelligible] is better [unintelligible] that always microscope is - I mean the diagnosis is [unintelligible].

02:42:25 MALE: I just wanted to make it a little bit more nuanced or interesting. And pathology is like 150 years old or so, but there are always new discoveries and new features that show up as important and that haven't been appreciated before. And once you sort of learn those, then how you look at an image changes completely, and I'll give you at least one example, which is that people have suddenly realized that involvement of nerves in prostate cancer is highly significant in terms of outcome.

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02:42:58 If nerves go in, then the outcome is much worse. And in fact there are trials going on treating - I kid you not - treating prostate cancer with Botox. And so the feature suddenly becomes not how many mitoses, but are there nerves, can you see the nerves in the cancer, and so that changes everything, you know, if it's true. And the same is true in colon cancer. Suddenly are there sclerosed - involvement of sclerosed veins around it?

02:43:24 And so what happens is that the veins, which used to be perfectly fine, the cancer goes in and then they almost disappear because they get surrounded by connective tissue and you ignore them, but you can find them if you look for them. And if you look for them and they're involved, then the prognosis goes down dramatically or it gets worse dramatically. And so again, a new feature which of course you would have to train either the observer or the computer to look at very carefully, and it changes the whole output.

02:44:00 MALE: I think we need to be clear about what we would be training the computer to do. So, in a

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situation where there are a number of mitoses, I think the grand challenge is that this is something that you can quantify specifically in the images. But as Cathleen was pointing out, this may not be how we are - the perceptual system is organizing our inspection.

02:44:27 So, is it possible to train the computer to recognize cases where there is a possibility of the number of mitoses sort of bleeding into some other sort of structure and flagging that in terms of like sort of a visualization of uncertainty? There's a potential here for this cancer cell to become sort of an embedded figure in some other structure, and because of this potential, this is what you should spend a little more time looking at or [unintelligible]. Are you optimistic about that sort of computer augmentation being possible?

02:45:01 MALE: I think we're all going to be replaced. I really believe it.

MALE: Great.

MALE: Good. [laughter]

[crosstalk]

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02:45:10 MALE: I'm very [unintelligible]. You know, and computers can do anything you want them to do. So, what you've described is sort of a cascading set of decision points or emphases. It makes perfect sense. I mean that's what humans do. They look, they make a decision, and they look for something else [inaudible] something else [inaudible]. They don't look for everything all at once. So, yeah.

02:45:31 FEMALE: So, let me interject the contrarian view. I don't think you're going to be - well, I don't think you're going to be replaced because - entirely. I mean it will be a different world perhaps, but what a computer has to be told - you have to make a decision again about how it's, you know, what is it looking for. So, if we had created a computer program based on - I'm not going to use the right words, but the what you were looking for before looking for nerves in prostate cancer, then it will be all built around that.

02:45:58 The early [unintelligible] of it might throw out information that it needed to identify those nerves



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because that was the relevant organization at that time. So, the computer systems are only going to be as good as what it is you tell it to do. Whereas, humans [laughter] well, yeah, that's the - again, I go back to then the training question. So, how are they being taught [unintelligible]?

MALE: Turn on your mic.

02:46:27

FEMALE: Okay. Good. So, can you hear me? Yeah? Okay, good. So, I'm Lalitha Shankar from the National Cancer Institute from the Cancer Imaging Program. I just want to talk very briefly about trainings that radiology and nuclear medicine residents get. So, obviously or maybe not so obvious is the first year and a half the student is expected to get a good sense of anatomy, right. So, gross anatomy or histology, which aids them in becoming reasonably efficient at becoming radiologists for anatomic imaging, nuclear medicine, for functional imaging, and for pathology.

02:47:06

So, going back to the radiology realm of things, you know, the students are trained on what is normal and then what is obviously abnormal. But then you get

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into a multiple sort of classification of symmetry if it's a subtle issue or lack thereof or if there's a lesion like you had at [unintelligible] so then you go into lesion size, you know, where is it spatially, what are the contours like, is that jagged or uniform because some things are cysts and some things are tumors.

02:47:37 We go into contrast enhancement. And then so this is sort of how we take it. So, then there's either bidimensional or volumetric assessments, all of that. So, then all of that, however, could have been a [unintelligible] fungal abscess too. So, that's where the clinical history comes in as to how did the patient present, et cetera. So, usually when you see a radiologist or a [unintelligible] report as in a pathologist report, you will say I see this, this, this, you know.

02:48:05 And there are some sort of - and I think Larry is going to talk about structured reporting this afternoon. So, there are certain things we expect to see in an adequate report. And that is followed usually with a list of potential diagnoses, and you

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go down as the probability decreases. So, you start with the most obvious or the most common thing you'd expect, but that's again based on both what the lesion is as well as the clinical history.

02:48:32

So, there's an amalgamation of information I don't think we have quite talked about here but several clinical decision support systems are trying to use, and they do that by looking at large databases of people with similar events or symptoms.

02:48:51

MALE: Could I make one brief statement? I think I've been listening to clinicians tell me that computers are going to put them out of business for 20 years or something. And it really has been harder to implement those things. There's a level of effortlessness to visual analysis that I don't think people account for when you go to write a computer program to do the same thing. So, I think it's, you know, [unintelligible] you may believe that they're going to put you out of business. I will believe that the day you show up at the FDA with a CAD device that is going to put you out of business, with the data to back you up to say that it will.

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MALE: Stand by.

02:49:35 MALE: You might not have to count mitoses anymore,  
but the whole diagnostic process is much more  
complicated than that one task.

MALE: You keep mentioning task, and I realize quite  
naïvely that I have no idea what the pathologist's  
task is. Who determines what scale they use? On  
average how many cells are on each slide? How long  
is the typical amount of time you spend on each  
slide? What are the basic statistics here?

02:50:11 MALE: Okay. So, I think the first thing to realize  
is that the tumor is this big, and the slide is this  
big and four microns thick. So, you're looking at a  
sample in the tenths of a hundredths of a percent of  
what's really there. So, it's a sampling issue  
first, but once you have the slide, then that's your  
universe and you look at that. And...

MALE: [inaudible].

02:50:39 MALE: Well, actually I mean pathology does encompass  
the growth and the micro. So, the tumor or whatever  
it is comes out, is looked at, and people can right

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away say that is renal carcinoma because grossly it just is. I mean it's a big white ugly mass on the kidney that shouldn't be there and it's eroding out through the capsule.

02:51:02 So, at that point you might be done, but there are lots of that microscopic diagnoses that have no growth clues. So, you then have to do the microscope, and you prepare the tissue by fixing it in formalin and putting it in paraffin wax so that you can cut it then. So then you have a uniform four or five microns thick section. And then you can look at cellular detail and also organization at the kind of larger than cells. People sometimes call them superpixels at basically low-power view.

02:51:35 And again, at low power many people can make the diagnosis. And the better you are, the fewer times you have to go to a higher magnification. And a lot of pathologists make the diagnosis by taking the slide, holding it against their white coat, and if it's very blue, it's cancer. Is that helping at all?

02:51:58 MALE: So, I'll become the contrarian [inaudible].

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MALE: The computer doesn't have a white coat. And then there are criteria. I mean all the way from does this look normal? Is it a normal breast lobule making, you know, that could potentially make milk or is it just a ragged assortment of cells all out for themselves? And that's sort of at a low-power view where you can just look at the organization.

02:52:27

And then you can go all the way up to a high power and say are features in the nucleus suspicious? So, there's nucleus and then there are little things called nucleoli. If they're big and red, that's bad, but that's a high power view. So, the criteria live at all these different powers. And most times it's actually a low-power diagnosis, which is why I'm sort of pushing back that, you know, ultimate imaging perfection isn't required because the tumors reveal themselves at lower power, and it's only occasionally that you need to go to high power to do anything useful.

MALE: Okay.

MALE: Is that helpful?

MALE: [inaudible]?

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02:53:12 MALE: It really depends on what the diagnosis is.  
For example, if you're looking for Helicobacter, you  
have to be at high power because they're little tiny  
things. So, that's a trivial example of you can't do  
it at low power because you can't see them, but  
oftentimes it's - I mean I think the world is  
[unintelligible] and you see the same kinds of  
information repeated at different scales.

02:53:37 FEMALE: [unintelligible] so then we can have a more  
detailed diagnosis and we can decide how to treat the  
patient and evaluate the patient's treatment.  
[unintelligible] using more [unintelligible].

02:54:07 MALE: I think [inaudible]...

02:54:16 ...people who are good at this or people who, you  
know, they say they want to go into pathology, they  
want to go into radiology, and after 10 minutes to  
three days you say [inaudible].

02:54:34 MALE: So, in my experience every expert domain of  
this sort from the NGA spy satellite guys to the  
radiologist to the airport security folks have that  
question, believe that there is an answer in the

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sense that they think that they know who's good and who's not good. So, again we'd have to ask what the gold standard truth is for are you a good whatever.

02:55:08 And to my knowledge, nobody has developed a convincing test, front-end test that will do this for you, at least not that uses the sort of factors that most of the people in this room are concerned with, right. So, you might think you'd be a better visual - be a better radiologist if you're better at, you know, sort of basic laboratory visual search tasks and things of that sort.

02:55:39 And actually there's some lovely experiments that suggest that expert radiologists are no better at Where's Waldo than the rest of us and so on. In principle, there should be something there. And everybody would love to have something because it's really expensive to train these folks, even the folks who turn over a lot like the ones at the airport. But I don't know of anybody who has successfully shown at this sort of cognitive perceptual-ish kind of level that they've got something convincing. But



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[unintelligible] looking at me like he knows the  
contrary.

02:56:16 MALE: No, not at all. In fact, I'm finding this  
terribly disturbing that this process is so  
haphazard. I mean I would think that - so, what  
you're talking about is that there are - when you're  
looking at a slide, you're entertaining some  
hypothesis for what might be out there. So, it seems  
like that is a very limited domain. There are  
relatively few hypotheses that you will probably be  
testing.

02:56:41 Each of these hypotheses should be - you should be  
able to characterize a sort of - well, I don't want  
to say optimal, but a good set of parameters for if  
this is the hypothesis you're entertaining, what  
would be a reasonable scale? It doesn't sound that  
intractable.

02:57:05 FEMALE: Try doing a few studies and you'll see how  
intractable it can be. So, when we were designing up  
the [unintelligible] trial, we insisted that the  
readers train in. There was a lot of controversy in

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the literature right about then about why did the studies published by gastroenterologists show that CT didn't work and the study published by the radiologists showed that it did.

02:57:29 And we thought that training had a big piece of this. So, we did a whole big training. Everyone was excited to come out. GE loaned us their space, their workstations, their teaching room, and people tested, including some of our PIs and people who were experts in the field who had developed the knowledge and developed the image processing.

02:57:51 And some of those experts had to test twice to pass. And other people who had never done it before but were interested came and did the training session and aced that exam the first time. So, if we could - yes, if we could figure out what differentiates these people, it would be great, but it caused so many problems.

02:58:14 MALE: Well, I think you put at least one finger on the issue that hadn't been mentioned at all, which is really the human dimension. And I'll give you an

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example that motivation, which is very hard to measure with ideal mathematical observers, is really critical. And so there was a study looking at - so, there's endoscopic yield. If you do a colonoscopy, can you - do you all know this?

02:58:42 Well, so there are two facts about colonoscopy. The first is that colonoscopy done in the morning has a higher yield than colonoscopy done in the afternoon. And secondly, there was a very interesting study where primary care physicians were given a little bit of training, enough to sort of navigate the scope and then they scoped their own patient. And their diagnostic, effective diagnostic yield was far better than trained endoscopists. Why? It was their patient. They cared. And so I challenge you to fit that into your sort of mathematical model.

02:59:25 MALE: And that being - when we had been talking to the Homeland Security folks, it seems likely that those sort of variables, what you might consider to be personality variables, probably have much more to do with your success as a bomb finder than whether your contrast sensitivity is really good. Look,

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you're not going to do well at any of these jobs if you're blind, but once you get, you know, to some sort of reasonable threshold, it's probably true that the test that you want ain't something that is coming out of our labs.

03:00:07 MALE: I mean, Richard, I think I completely can see your point, which I think is also Brandon's point that there's so much variability among the different raters [ph.] that it's, you know, swamping in many cases all else. But so perhaps that is the point where some benefit might be gleaned from the computer vision. So, if there is so much variable in the human raters [ph.] that you can't even settle on some basic parameters, then try to train a classifier to make some of these diagnoses that you're talking about.

03:00:43 And from that classifier, it will be able to suggest an optimal viewing scale. And you can see whether that sort of optimal viewing scale corresponds to, you know, then do the study and see whether that translates into some detection benefit.

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03:01:00 MALE: I've actually worked in this area for quite a while.

MALE: Whoops. Sorry. [laughter]

MALE: I even have [inaudible] and commercial instruments have come out [unintelligible] being sold by [unintelligible], and I also have a really good name for this for like digital imaging. Part one of the [unintelligible] have this giant field of view. Wouldn't it be nice if the computer popped up and sort of ticked five or six regions that were most salient and then magnified them for you? So, I call that pre-zoom [ph.]. Thank you. Thank you.

[laughter] So, yeah, I mean I'm definitely on the same wavelength.

03:01:39 MALE: Yeah. I don't know if you're the guy with the patent on it, but for reading cervical cancer screens for pap smear tests, which are basically a visual search task with thousands and thousands of little cells spread across a slide, my understanding of the way that computer-aided detection works there is that it looks at the image and basically tells you if there's not something in these top 30 little tiles out of the many hundreds that we could get, then you

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can move on. And there's the place where the computer-aided detection piece is - seems to be really useful as I understand it. Is that yours?

03:02:29 MALE: ...[inaudible] which we haven't really - I wanted to hear from the people who are designing these studies again sort of attentional stuff. It's not realistic to have a study with 50 percent normal and 50 percent cancer because in the real world it's 99 percent normal and one percent cancer depending on the situation. But you can't get radiologists to sit down and look through 10,000 cases to get decent numbers. So, how do you map that into a realistic state?

03:03:03 MALE: Well, that was the whole idea of our [unintelligible] analysis was that if they fundamentally change the way they detect things based on prevalence. That's really the strong prevalence hypothesis. Right. I would call maybe the weaker prevalence hypothesis that they simply shift where they are on an ROC curve. You can debate about that, but at least a lot of the evidence in a lot of cases says that when we do - you can at least show that

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people will move on what appears to be an ROC curve,  
taking away that concern.

03:03:36 Now, there may be other cases where they don't. And  
you can imagine like one of the obvious causes for an  
actual shifting, it would just be vigilance. If  
you're doing one out of a thousand and you just get  
tired and you start clicking go, go, go, go, go, go,  
go, now your performance is going to drop through the  
floor, but it's strictly an issue of vigilance. I  
don't know if we should be building that into device  
evaluation. [inaudible]

03:04:00 MALE: But that's the real world. That's actually  
what's going to happen when they hit Topeka [ph.].

03:04:10 MALE: I guess - I guess - well, I don't know because  
you're talking about a laboratory study versus your  
clinical practice where you've got a clinical  
management decision, you got your malpractice  
insurance, you got all - you got to give a report.  
You got a lot of other things that there's enough  
differences between the laboratory study environment  
and the actual clinical environment that it's not

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clear that a vigilance defect [ph.] at the laboratory necessarily translates to a vigilance defect [ph.] in the clinic.

03:04:36 MALE: Well, let me just chime in one thing. There's many phases to the technology. The early phase is where you're just trying to make sure that it actually does an image and it could show the most obvious of obvious pathology. And then there's the ones where you're trying to figure out how it will fit into the workflow. And then there's the ones where you're trying to get it to the FDA. And then there's the ones where you're seeing it in the real world.

03:05:00 And you got to ask yourself where am I asking the question, and if you're asking the question about vigilance, that is in the real world where they're dealing with the real race [ph.]. When we're talking about the FDA, that's the technology. Is the technology doing what it's supposed to do? And can the users use that information the way they're supposed to use it? And then if it's early, just



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does it work? Is it there when you want it to be  
there in the most obvious of situations?

03:05:30 So, you got to think about that entire phase of  
technology evaluation. And then there's a last one,  
and that's do we want to pay for it as a country?  
You know, that's when you're really looking at the  
epidemiology results and you're trying to think of  
how much things cost. And so this is a big spectrum.  
And not everything, every evaluation fits that entire  
spectrum.

03:05:52 FEMALE: [inaudible] long over time. Sorry. Did you  
want to first?

MALE: [inaudible].

FEMALE: Okay. So, I'll bring it to digital  
mammography, which when people first started talking  
about it, there was this whole question, can we just  
say that the camera takes a picture or do we have to  
prove that the radiologist can use the information in  
that picture? And it ended up being de facto because  
GE filed their PMA that we had to prove that the  
radiologist could use the information.

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03:06:22 So, that's where it sat at FDA for many, many years. The GE PMA was approved the end of 1999, and it wasn't until was it 2009 that the [unintelligible] came or maybe even later that the [unintelligible] came from having to prove safety and effectiveness for the radiologist using the information to saying okay, by now with four approvals and 10, 15 years in the market we know enough to say that if the images looked good, the radiologist can use it. So, it does evolve.

03:06:54 MALE: And if the technology specifications fit what we've seen before, then that's the pathway now is to do technology specification measures, the [unintelligible] measurements, show some sample images that it's not something else isn't going on. That's how mammography makes it through now, digital mammography.

03:07:18 MALE: Going back to the prevalence thing, which I sure hope is why Miguel is pointing at me. I'm not quite sure what [inaudible].

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03:07:30 So, it's of course absolutely true that you can't go and ask radiologists to read at, you know, one percent prevalence because there's not enough time and money in the world to do that. So, we do these prevalence studies in the lab because you can ask, you know, poor schnooks off the street to do it for 10 bucks an hour. When we've done that, it's clear that a big piece of these prevalence effects are exactly what you're describing as criterion effects.

03:08:00 You don't successfully model it unless you also include a - what's almost like a satisfaction of search notion that you're changing the time at which you're willing to quit a search. And another one of the wrinkles that you certainly know about but other people who are playing around in signal detection land in the lab may not is that the model that you need for - your signal detection model needs to be an unequal variance model.

03:08:33 The slope of the zROC function is not going to be one. In these things it tends to be less than one. And you've kind of got to make the assumption that it really is aligned in some sort of these space because

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it's really, really, really hard to get enough  
experimental power at really low prevalence. You can  
do a pretty good job in the lab of modeling this  
stuff. And now Miguel, who was waiting for me to say  
that so he could say...

03:09:05      MIGUEL ECKSTEIN: No. [unintelligible] I think  
there the original question is there's, you know, and  
this has been a concern before. In the real world  
the prevalence is low, but most observer study we  
can't afford to run those studies with a radiologist.  
So, we have what's called an enriched dataset. And  
the question is does that enriched dataset with a 50  
percent prevalence and you're doing image quality  
evaluation with that, how does it actually translate  
or relate at all to the real clinical case where the  
prevalence is [unintelligible]?

03:09:36      So, at one side you have stuff with like Jeremy that  
says, you know, he's showing that these prevalence  
effects have a large effect. I think we agree that a  
lot of it is a criterion shift, but he I think  
[unintelligible] have data saying that maybe there's  
something else additional. Although, I think it's

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unclear how that translates also to, you know, rather than undergrads or people, to actual radiologists which have a different set of utility function.

03:10:05 But then there's also, you know, literature by David [unintelligible]. He had a [unintelligible] sort of in the - I think it was in the early '90s. And one was called [unintelligible] prevalence effect. And he did the ROC studies with [unintelligible] radiologist. And he said that it is mostly [unintelligible] and so as a ballpark, you do - using an enriched dataset is okay at the first [unintelligible].

03:10:35 The second effect he actually was concerned about was something he called the laboratory effect. So, that's not a prevalence, just a fact that when you actually do an observer study, people are, you know, most of the time know they're part of an observer study. This is not their clinical practice. And how would that affect? And I think the outcome was I think yeah, things change and, you know, it's not as great as actually putting them, you know, them

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participating in something that they think is  
actually part of the clinical reading.

03:11:05 But I think for the most part he actually came to the  
conclusion that that actually was for the first, you  
know, for the most okay too. So, are they perfect?  
No, they're not perfect. But, you know, what is the  
alternative?

03:11:19 MALE: We had a really interesting problem with this.  
We did a prevalence study with mammographers. And  
the way we did the low prevalence part of this is we  
slid cases where we knew the gold standard truth into  
clinical practice at, you know, very, very low rates.  
And so there they had consented, but they did not  
know that they were in the laboratory. And we  
compared that to a set of an enriched stack that they  
read in the laboratory.

03:11:48 They made many more miss errors in clinical in the  
low-prevalence clinical case than in the laboratory.  
And people - the radiologists complained to us that  
against what might be our intuition, they thought  
that the radiologist might have worked harder in the

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laboratory case. You know, in the clinic they're supposed to - they're merely saving lives. In the laboratory case somebody's going to tell whether they're right or wrong. [laughter] It was kind of...

03:12:19 FEMALE: Not just right or wrong, but how did this reader compare with that reader? They always want to know that.

MALE: They are an amazingly competitive group of people. They are scary competitive.

03:12:29 MALE: I have somewhere on my computer I think a paper that I haven't read, but I think the title says it all. If you don't see it often, you often don't see it.

MALE: That's an excellent paper. I really like that paper. [laughter]

03:12:47 MALE: When I heard Miguel say it's not so bad in the laboratory effect or the prevalence effect are not so bad, what does that mean? And let me chime in on that, and that is when you're trying to make comparisons of two modalities. That's really where it doesn't have the biggest impact because that bias

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lives in both modalities whether you're in the clinic or whether you're in the lab. That's my first point.

03:13:15 The second one is I guess a little advertisement or notification. We've been working on a large reader study with mammography versus digital versus screen for the patients that have dense breasts. So, this is the situation where we might actually expect a difference between digital and screened film.

03:13:39 And we are probing several different prevalence settings, 50 percent, 30 percent, and 10 percent. Ten percent isn't half a percent, but it's at least we have some contrast from 50 percent. And it's going to have 20 readers in each of these modes and a pretty nice sample size where we're actually expecting an effect.

03:14:03 So, not only will we - we're using the images from the [unintelligible] study so that we can now not just link it in terms of all laboratory studies; we're going to be able to link it to the [unintelligible] perspective clinical trial to show that the ranking of these two modalities hopefully is



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preserved when you go from the clinical trial to this laboratory study because that's - I've gotten the question where is that study that demonstrates that these laboratory studies mean anything in terms of clinical practice?

03:14:37 The first thing I'll say is don't ever expect the sensitivity or the AUC [ph.] in your lab studies to equal what you will see in the clinic because there's no skin on the line or there's competitive issues or whatever or the technology hasn't even been disseminated when you're doing these lab studies. So, don't expect those absolute measurements of performance to hold, but my core [ph.] tells me that we can compare two modalities and get the same comparison results in the lab as you can get in the clinic.

03:15:10 And so that's where the hypothesis [unintelligible] there, and either it will be confirmed or I'll have to acknowledge that it's not confirmed. And I'll tell you what, if it's not confirmed, clinical trials might pay the price of that result. So, we'll see how it goes. And data collection is to be done in

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March. And when it's all said and done and the first paper or two are done obviously and even before then, data sharing with the government. I believe in data sharing. So, those results and raw scores will be available.

03:15:47 MALE: I couldn't agree with you more in terms of the power of those tools to compare two different technologies. But I wanted to point out how different radiology is from pathology because pathology, 90 percent of everything is on that physical slide. It's already been stained and processed and everything. And then the - only the technology is it's taking a picture. And so the question is is taking a picture which looks on the screen almost like what you see under the microscope, is that better or worse?

03:16:16 And my point is the difference, the sort of leveraged power there is very small because all of the hard work has been done before the technology sets in. It's just a camera. And so that's why I'm suspicious that it doesn't merit all that scrutiny because I think it's sort of intuitively good enough. And

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there may be at the margin like in cytology at 100X  
it may not work as well as a microscope where you can  
focus up and down.

03:16:44 But just to point out that pathology is a different  
problem than radiology and doesn't map exactly the  
kinds of things that you're doing where the  
technology basically is the image. It's, you know,  
the x-ray, the contrast, everything, it all lives in  
the box.

03:17:03 MALE: Just to respond a little bit to that, you  
know, you got to understand that FDA's going to be  
concerned. What's going to happen? You're going to  
deploy it to the United States. And when we talked  
early on and presented at a panel meeting on this  
topic early on, you know, we talked about the risk of  
if this imaging modality wasn't as good as just  
taking a picture.

03:17:26 And it drives treatment. It makes final diagnoses.  
These are really impactful decisions. So, the  
sentiment was that it is a high risk, new technology,

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and so it's really - that in front of people makes  
caution kind of the default way forward.

03:17:54 MALE: Richard, I was a little surprised to hear you  
say that there really is no great benefit of a new  
technology in the pathology or did I misinterpret?

MALE: No. That's not what I said. What I'm saying  
is that the impact on the experience of the  
pathologist between looking through a microscope and  
looking on a screen on an image taken through a  
microscope with a camera is much smaller than the  
difference between film and digital and tomosynthesis  
and MRI and functional MRI. Okay. So, I'm just  
saying it's a part of the thing, but it's a very  
small part in my estimation.

03:18:34 MALE: So, I'm just getting your opinion. So, maybe  
your...

MALE: By the way, most pathologists will probably  
agree with me and the experience where it's been  
deployed without the benefit of FDA blessing. Like  
in Canada, they love it. It works great. And, you  
know, they did their own validation studies. They  
didn't just march in blindly. They made sure it

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worked, but the point is it does work, and I think  
that we can sort of go from there at least.

03:19:03 FEMALE: I fear that there's a danger to us. I think  
[unintelligible] images [unintelligible] danger  
because I can see some risk because [unintelligible]  
imaging is really good. And the [unintelligible]  
validation study [unintelligible] quality of the  
image [unintelligible] percent of [unintelligible]  
out of focus.

03:19:41 So, most of the time, I think that the out-of-focus  
area [unintelligible] diagnosis, but we don't know  
when it happen [unintelligible] diagnostics. So,  
that's why we are [unintelligible] sometimes.

03:20:03 MALE: Maybe your zoom lens model already does this,  
but do you think it would be valuable if the  
resolution started to increase with fixation  
duration? So, the longer you end up looking at  
something, slowly you get a better high-resolution  
view of it?

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- 03:20:24 MALE: No. Because people who look at high power, who spend more time at high power actually perform less well on [inaudible].
- 03:20:33 MALE: So, [unintelligible] coming through a sort of filter of lower power. You start off at lower power and then once you're - over time, over those few hundred milliseconds you're getting an increase in power.
- MALE: It's a testable hypothesis.
- 03:20:49 KRISTIN LITZELMAN: I'm going to take one more comment and then we're going to wrap up.
- 03:20:52 MALE: [inaudible] disciplines that also use medical images, and ophthalmologists look at retinograms and [unintelligible] vascular surgeons look at the angiograms and so forth.
- 03:21:08 KRISTIN LITZELMAN: [inaudible].
- 03:21:29 [BREAK]
- 04:25:33 [BREAK ENDS]

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04:25:34 MALE: And in general I'd like to say that first of all, it's been going really well. It's been exceeding my expectations. You guys have been doing great. We have a lot of diversity of perspective, scientific perspectives here. And what I would like to see in the lunch session, in the post-lunch session is people who have not been talking as much to please jump in more and people who have been talking a lot to please jump in a little less.

04:26:04 I'm not picking - I mean no, really, the discussions have been fabulous, but I really do want to take advantage of the fact that we have a lot of expertise here. And to that end, I think one way to get us sort of back into the intellectual atmosphere after lunch is just to have people go around and briefly introduce themselves and what they do. So, maybe starting with Alicia and just going around the table.

04:26:33 MALE: No.

04:26:42 ALICIA TOLEDANO: Okay. So, I just think that the two ladies to my right are doing really important jobs here today and we should recognize them. So, we'll do that first. [applause]

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MALE: I'm sorry. Yeah. [unintelligible] and  
Courtney. Do you want to introduce yourselves?

FEMALE: We are just [unintelligible] and Courtney  
from ICF International with the communications team  
here.

04:27:07 ALICIA TOLEDANO: Great. So, I'm just Alicia  
Toledano. I'm a biostatistician. I've been working  
in imaging I guess, what, 20 plus years now, 22, 23  
years now, mostly radiology, although I've worked  
with a product that does skin lesion imaging, which  
is kind of cool and some CAD techniques and  
statistically with correlated data and also working  
more recently with the radiology societies,  
Quantitative Imaging, Biomarkers Alliance trying to  
come up with the right terminology and think about  
ways to evaluate quantitative imaging biomarkers,  
what can we take from laboratory science to bring in  
and how can we capitalize on the information in the  
biomarkers. Maybe that was too long.

04:27:55 MALE: Yeah. A slightly briefer summation of what  
you do.



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- 04:28:01 FEMALE: [inaudible]
- 04:28:23 LALITHA SHANKAR: I'm Lalitha Shankar. I'm the chief for the clinical trials branch in the cancer imaging program at NCI. We're situated in the Division of Cancer Treatment and Diagnosis, but my personal interest has me working with DCCPS for basically post-marketing sort of activities to see how well the tests do after your phase threes as well as the Division of Cancer Prevention.
- 04:28:50 RAGINI VERMA: Hi. I'm Ragini Verma. I'm from UPenn Radiology. So, I do [unintelligible] neuroanatomy. So, a lot of structural and functional networks [ph.] for mainly schizophrenia and autism and now a whole lot of brain tumors.
- 04:29:09 ALEJANDRO LLERAS: Hi. I am Alejandro Lleras from the University of Illinois, and I do work on vision and visual attention most.
- 04:29:17 CATHLEEN MOORE: I'm Cathleen Moore at University of Iowa, and you already saw what I do.

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- 04:29:23 YUKAKO YAGI: I'm Yukako Yagi. I'm from Massachusetts General Hospital and Harvard Medical School, and I've been [unintelligible] at the older kind of technology [unintelligible].
- 04:29:41 JEREMY WOLFE: I'm Jeremy Wolfe. I'm in the Department of Ophthalmology and Radiology at Brigham and Women's Hospital and Harvard Medical School, and I do visual attention, visual search.
- 04:29:54 EDWARD VUL: I'm Ed Vul. I'm in the UC San Diego Psychology Department, and I work on [unintelligible] models of human cognition, including visual attention.
- 04:30:05 NICK TURK-BROWNE: I'm Nick Turk-Browne. I'm in psychology and neuroscience at Princeton University, and I work on visual learning and memory and attention.
- 04:30:16 RICHARD LEVENSON: I'm Richard Levenson at UC Davis, and I use some optical training to allow me to focus on everything. But new kinds of [unintelligible], new kinds of multiplexed imaging where you can do a

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hundred different antibodies at once on tissue and something I'll tell you later this afternoon.

- 04:30:38      MIGUEL ECKSTEIN: Miguel Eckstein, University of California, Santa Barbara, and I've for some years now have split my time between doing basic vision science and medical imaging perception.
- 04:30:51      MATT PETERSON: I'm Matt Peterson. I'm at George Mason University. I wear three hats there. I'm in the Human Factors Group, the Cognitive and Behavioral Neuroscience Group, and the Neuroscience Group, and I do anything related to attention, including visual search and eye movements and even some neuroergonomic human factor [unintelligible] stuff.
- 04:31:09      GREG ZELINSKY: Hi. I'm Greg Zelinsky. I'm at Stony Brook University in psychology. I use eye movements to study how people search for things, and in computer science I study how computers can detect categories of objects.
- 04:31:26      JAY HEGDE: Hi. I'm Jay Hegde from Medical College of Georgia [unintelligible] Regents University. I

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study perception and action [unintelligible] in  
humans and monkeys.

04:31:40 CRAIG ABBEY: I'm Craig Abbey from UC Santa Barbara  
also. I'm trained as an applied mathematician, and  
I'd say my interests are in how information,  
diagnostic information, is extracted.

04:31:54 ANDREW MAIDMENT: Andrew Maidment from the University  
of Pennsylvania. I'm in the Department of Radiology.  
I'm the chief physicist for the University of  
Pennsylvania Health System. My research, as you saw  
today, I develop x-ray imaging systems predominantly  
for breast imaging, and I use perceptual tools in the  
development process.

04:32:14 VINAY PAI: I'm Vinay Pai. I'm the acting division  
director for the Division of Health Information  
Technology at NIBIB [unintelligible].

04:32:23 REBECCA FERRER: I am Becky Ferrer. Like Todd, I am  
a program director at NCI. I actually study emotion  
and decision making. So, I don't have any expertise  
in vision science, although I did use an eye tracker

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in an experiment once. But that is not why I'm here.  
I am here for my skills in moderating, which involves  
looking at this clock. I can hold up signs other  
people have made, and I have been known to clap at  
people over the time when I [unintelligible].  
[laughter]

04:32:54 MALE: Back row? [laughter] The guy laughing.

04:33:01 FRANK SAMUELSON: I'M Frank Samuelson. I work for  
the FDA in the Division of Imaging. And I work with  
Brandon Gallas.

04:33:14 ADAM WUNDERLICH: I'm Adam Wunderlich. I'm also at  
the FDA. I primarily work in statistical methodology  
for reader studies and also with model observers.

04:33:30 MALE: I'm [unintelligible] Pazesh [ph.] also from  
the FDA. I do [unintelligible] development for  
[unintelligible] vision and machine learning, which  
for medical applications means developing CAD and  
[unintelligible].

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- 04:33:46 MALE: My name is Jerry [unint], and I'm in the Office of the Associate Director of the Behavioral Research Program at NCI.
- 04:33:57 BRANDON GALLAS: I'm Brandon Gallas at the FDA [unintelligible] my colleagues over there. Did some model observer stuff as a graduate student trying to understand how well we are able to find white blobs [unintelligible].
- 04:34:19 PAIGE MCDONALD: Hi, everyone. I'm Paige McDonald, and I'm chief of the Basic Biobehavioral and Psychological Sciences Branch, the branch that's sponsoring this meeting. So, thank you, guys, for coming and sharing your intellectual expertise. It's been really fascinating thus far.
- 04:34:36 ANNETTE KAUFMAN: Hi, everyone. I'm Annette Kaufman. I'm a program director in the Tobacco Control Research Branch at NCI. I, like Becky, have done one eye tracking study. And I'm mainly interested in risk perception and I'm currently looking at the national lung screening trial. So, a lot of what

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you're saying here applies to that work that I'm  
doing. So, thank you all for being here.

04:35:01 MALE: And last but not least, our speaker.

04:35:13 RAJ RATWANI: All right. Good afternoon, everybody.  
Sorry for missing the first half today, but I'm  
looking forward to catching up with everybody this  
afternoon and into tomorrow. So, my name is Raj  
Ratwani. I serve as the scientific director for  
MedStar Health's National Center for Human Factors in  
Healthcare. That's a mouthful. Also  
[unintelligible] at Georgetown University in the  
Department of Emergency Medicine. So, a little bit  
about my background is in human factors with a big  
slant at cognitive science. Matt Peterson was  
actually on my dissertation committee. Is that on?  
There we go.

04:35:44 Matt Peterson was actually on my dissertation  
committee several years ago. I probably know about  
10 percent of the people in this room. So, I'm  
looking forward to getting to know everybody else at  
some point. So, I wanted to start with a little bit

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of background about our center and kind of how that frames the problems that we try and address.

04:36:01 So, our center is about four or five years old. We are part of MedStar Health, which is a 10-hospital system in the Mid-Atlantic region. It's actually the largest in the Mid-Atlantic area. And to give you an idea of what I consider our research playground, our laboratory, here are a few numbers: 10 hospitals plus a whole host of outpatient services; 30,000 associates, all of which we have access to for research purposes; 10 hospitals under one IRB, which people that have dealt with IRB, which is pretty much everybody in this room, realizes how important and how much of a benefit that is.

04:36:35 It includes teaching hospitals, everything you can name. The way that I sell it is it's a microcosm of the American health care system. So, urban hospitals, suburban hospitals, rural hospitals, you name it, we kind of do it. And to give you some of the numbers here, over half a million ED visits. So, it's a pretty large system with lots of access [ph.].



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04:36:55        And what our center is focused on is patient safety, quality, and efficiency very generally, and more specifically for this group is we're looking at imaging and non-imaging and ways of optimizing a lot of the work that we do in those areas. So, I'm going to very briefly talk about kind of two core research questions and then one a little bit of data, and I'm not going to go too heavy into data.

04:37:18        So, the first big piece for us is how can we really improve sort of clinician perceptual-cognitive processing, reducing error, improving efficiency? We have access to large simulation centers as well. We have lots of medical students and residents that come through our system. So, we're very concerned about enhancing learning and ensuring that learning perpetuates throughout the career of a clinician.

04:37:40        The second big piece is how can we actually develop more innovative training solutions? So, when we look at what happens at Georgetown University as a medical school, which is an incredible medical school, there has been a tremendous amount of advancement in the actual training of med students at a very general

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level. So, we're looking at ways of enhancing that process as well.

04:37:59 And so I was asked to talk about some of the non-imaging work. I think most of us are probably focused on imaging. For us that includes looking at individual displays. That could be anesthesiology machine displays, displays that you find in the emergency department, patient-tracking dashboards, et cetera, and also the outputs of diagnostic tests. And so one of the experiments I'm going to talk about is some work that we've done with ECGs.

04:38:21 And two active projects that we have going on right now, one is the ECG work I'm going to talk about in a minute. The second is looking at how anesthesiologists maintain situation awareness in the OR. So, we're studying that project now, taking [unintelligible] trackers, putting them on anesthesiologists at different levels, and seeing how they perform. So, we're very much on the applied side and want to do as much as we can in the clinical environment or in simulation and transition that to the clinical environment.

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04:38:48        So, for the particular data I want to talk about, one of the big studies we have going on right now is looking at how attending emergency physicians, well-experienced emergency physicians, and resident emergency physicians interpret electrocardiograms. So, in our system a physician, an emergency physician will likely look at somewhere between 7 and 10 ECGs per hour at a heavy-shifting [ph.] emergency department.

04:39:12        The way incentives are set up is they need to read those ECGs as quickly as possible and in fact are interrupted, whatever tasks they're doing are interrupted to view that ECG. And error rates are high variability but anywhere between 5 and 50 percent if you look in the literature, depending on the type of anomaly that's trying to be detected in the ECG. So, we have been doing two things. One is trying to develop eye movement based models to actually predict accuracy, and you can see some of our performance here, which is not fantastic. We're looking at about 78 percent accuracy or so. I think we can do better.

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04:39:43        So, one is looking at how we can actually predict ECG interpretation accuracy. And the second is looking at differences between the attending physicians, the well-experienced physicians and the residents and seeing if we can use that information to bolster training. So, I mentioned how training is still kind of way back where it was 20 years ago. Traditional ECG training is read a textbook and then learn it on the job kind of thing and optimize on the job. And I think we can make tremendous advancements there. So, this is one of the areas that we're going into. So, I'm going to stop there and hopefully [inaudible] discussion [inaudible]. [applause]

04:40:28        MALE: Just I wanted to hear a little bit more about the eye tracking models. It seems like ECGs are highly variable in terms of where the relevant features are in the display. So, it couldn't just be a simple model of if you look in the top left, you'll do better, right? It's something more about the pattern of eye movements?

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04:40:45 RAJ RATWANI: It is. Yeah. I didn't put the predictors up there because it's still very new work for us, and we weren't quite comfortable sharing that. But yes, it is. It's looking at essentially some measures of attention, how narrowly they are focused in particular areas and then the sequence of patterns that ensue after an initial screening period. And we can use lots of help on this. So, if there's folks that are interested in collaborating - I'll should tell you from the outset, we're a young center with lots of problems to tackle and are happy to collaborate across the board.

04:41:17 MALE: I wonder if you could tell us a little bit more about what the features are that people are looking for in this [inaudible].

04:41:26 RAJ RATWANI: In terms of the ECG?

MALE: Yeah.

RAJ RATWANI: So, I used to have a slide that sort of delved into ECGs in more detail, but there's 12 different leads to the ECG, and I think they correspond basically to these boxes. And so from the emergency physician's perspective their obligation is

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to determine whether there's a threat of a heart  
attack or not and then very rapidly make a decision.

04:41:50 So, it's very different from cardiologists that are  
doing a very deep inspection of the ECG to look at  
any kind of heart problems. So, in terms of what  
they look for is there's the PQRS wave, which - let  
me see if this mouse is active. So, they will look  
at several of these different specific wave forms and  
see whether they can detect a particular anomaly  
compared to what would be standard. And each of  
these different leads, time goes across the X axis.  
So, these are - they look at - basically it's  
actually a different timeframe from this lead.

04:42:22 So, they're getting a snapshot of the time that that  
ECG is taken and then will look across different  
leads to determine whether there are particular  
anomalies that will correspond to various aspects of  
the heart that would be demonstrating that. Sort of  
a very rough description. So, you can think of each  
of the leads as a different camera shot or snapshot  
of functioning of the heart. If folks have a better  
explanation, please chime in.

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04:42:49        So, yeah, so what we've done is we've sort of created what we would consider a gold standard. So, we have a panel of about three experienced emergency physicians that will then rank each - will then basically grade each response. In each response here there's a different quality of responses, but it would basically be would the emergency physician triage the patient in the appropriate manner based off of [inaudible].

04:43:12        MALE: So, if I'm looking at reading this right, if you just classify everything as correct, you'll get 76 percent accuracy, and you're at 78?

RAJ RATWANI: That's correct.

MALE: What would be a - like how much better than 76 percent accuracy would you need to be for this to be useful?

MALE: [unintelligible] to how this would be used?

RAJ RATWANI: Yeah. So, we're about 74. I think, you know, average actually is about 74 percent, right. We're at best 78 percent [unintelligible]. And we, so [unintelligible] not a very strong model and we haven't spent a lot of time actually

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developing the model, but I think we can do  
considerably better.

04:43:42 In terms of what would be useful in actual  
implementation is a great question. I'm not quite  
sure, right. So, if you look at radiologists and  
their interpretation in mammography and how much they  
rely on those particular algorithms, it varies  
tremendously, and most of the time they'll just say  
well yeah, we look at it, but then we do our own  
interpretation. And even with ECGs there's automated  
computer interpretations. Physicians are instructed  
not to pay attention to those. They still do and it  
includes decision making. I don't have a strong  
answer for you on what would be, you know, if we can  
get to 80 percent, it's going to be golden and we can  
get it in the environment.

04:44:17 FEMALE: I have a question. So, I'm guessing that  
what's on the slide is some [inaudible]. So, are the  
[inaudible], for example, that part of it that's red,  
is that the diagnostic part of it?



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04:44:34 RAJ RATWANI: So, the question is that you're saying red - so like in a heat map like this blob right here? So, the challenge is that each specific lead may or may not provide diagnostic value for a given abnormality, right. So, under certain circumstances this may hold value, and under other circumstances it may not.

04:44:56 FEMALE: [inaudible]?

RAJ RATWANI: This particular aspect, yeah.

MALE: So, can you help me recruit readers for imaging studies?

RAJ RATWANI: We potentially could. Yeah. Yep. I'm happy to talk offline about how we could do that.

04:45:20 MALE: Can you look at this from like an informatics point of view? Do you know how much time they should be spending in each box? Because if I sort of take that bottom region as four boxes because it's bigger, there's 16 boxes. They should be spending about 6 percent time in each. And from those data it seems like they're spending about 6 percent time in each. So, that means that [unintelligible]. I mean can you train them as to which one has more information?

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04:45:46 RAJ RATWANI: Right. So, I think the challenge here is what we're finding is that in the first - in lots of [unintelligible] perception kind of work and even graph comprehension is the first few seconds is this very rapid assessment to determine where the important aspects of the ECG are. Then after that it's sort of a more controlled deliberate approach of looking at particular leads and then continue through the process leads. So, I think the notion that they would be spending 6 percent in each particular cell is not quite accurate.

04:46:24 FEMALE: So, the [unintelligible] it shows that this is where most of your emergency physicians will come and exactly take a look and that's how you make a decision?

04:46:32 RAJ RATWANI: So, perhaps the [unintelligible] was not the right [unintelligible]. This is one quick snapshot of a particular emergency physician for a particular ECG. This pattern may be wildly different for a different emergency physician. And in fact if you look across experienced emergency physicians,

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there's a tremendous amount of variability in the process. There's a lot of internal consistency within the participant, but across participants it's quite variable.

04:47:02 MALE: I mean this is rolling in time too, right. So, it's taking a snapshot and then [unintelligible] it's a dynamic process.

04:47:10 RAJ RATWANI: It is a dynamic process, but in practice they're handed either a physical piece of paper, so it's a snapshot, or in some more advanced systems would be an electronic version of it. But they're not - the emergency physician itself is not looking at a rolling ECG. That would happen either in the cath lab further down the line or by the cardiologist, depending on how the patient is triaged. That's a good question.

04:47:36 MALE: [inaudible]?

RAJ RATWANI: Right. And lack of data [unintelligible]. So, yeah.

FEMALE: [inaudible]

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04:48:06 RAJ RATWANI: It depends on the particular  
abnormality. So, for certain abnormalities, the  
computer algorithms are absolutely horrific. And  
those also generally tend to be the ones that the  
human observers tend to miss, right. So, it's the  
[unintelligible] kind of issues that we run into.

04:48:29 All right. Thank you. [applause]

04:48:42 MALE: All right. The next speaker will be Miguel  
Eckstein.

04:49:16 MIGUEL ECKSTEIN: Okay. Thanks, Todd, for organizing  
this. This is a little bit of a dream for me too  
because [unintelligible] so it's nice to have people  
from both fields in the same room talking these  
things. So, the challenge was to have one slide, and  
I was - and my challenge was also to sort of  
summarize my work in both fields in a single slide.  
But because I saw the list of people and I saw  
there's a lot of vision scientist people, vision  
scientists, fewer medical image perception people so  
I sort of took the position that I think it would be  
really useful so instead of going to my research in  
one slide, I have to go through a hundred years of

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medical image perception in one slide. So, it's  
going to work out great.

04:49:54 So, there's a limit on slides. There's a limit on  
time. There's not a limit on words so I'm going to  
speak really fast. Okay. So, I think it's fair to  
say that it's been a struggle to have people accept  
that the imaging chain does not stop with the image  
creation, but that it really continues, you know,  
once the, you know, if it's an image [unintelligible]  
radiologist, it continues through the process  
[unintelligible] of the observer.

04:50:22 But I think there are many examples through time to  
demonstrate that understanding vision has important  
contributions to [unintelligible] interpretation.  
I'd like to - some of you know this, but I think this  
is a classic example, and it's a beautiful example.  
So, when x-rays were introduced, the first imaging  
systems were these [unintelligible] that were  
actually very, very, very dim. They were so dim that  
you actually would not - could not rely on cone  
vision. You actually relied on broad vision.

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04:50:49 [unintelligible] actually related sort of basic studies in vision science with psychological behavior and had an explanation for this. And so that radiologist had to actually stay 20 minutes in the dark to actually [unintelligible] because otherwise he would not see a thing or have the other option then to introduce what's called the adaptation red goggles. We can talk about later about how that works, but that really was the reality. If you just came in [unintelligible], you could not see a thing.

04:51:19 And this went on until actually imaging [unintelligible] were introduced and these [unintelligible] that were invented by [unintelligible] were actually [unintelligible]. So, there's one example. It's a great example. Here's an example that is sort of one of the first projects I worked on. And looking through [unintelligible] one example where I think, you know, perceptual [unint] have an impact. I thought it was very simple. [unintelligible] when I collected this data.

04:51:45 So, what you there is actually a little cropped clip, a cropped part of what's called a [unintelligible]

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coronary angiogram [unintelligible] of x-rays of the arteries of somebody's heart. There's a contrast agent that's injected, and that's why you can see the artery. And it's typically until recent, until the '90s, these were actually [unintelligible]. And you can see that there's some noise in these images [unintelligible] images are limited by the quantum noise because you want to have a limited dose on patients.

04:52:17 And one thing that we knew from vision science is that you want to play these movies really fast to try to integrate that noise away. If you play them really fast, you can integrate that noise. But the problem is that there's motion. So, when doctors try to do this with film and they try to play it really fast to integrate a noise, what would happen? [unintelligible] were actually [unintelligible] moves very abruptly. So, how do you solve that?

04:52:40 Well, you were able to digitize these images in the nineties [ph.] for the first time. What you could do is actually have a tracker that digitally stabilizes the artery and you could actually do something like

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that where you basically shift the frame so you actually visually stabilize the artery. It would allow you to display that at a very fast rate and integrate the noise away and not have this problem with tracking.

04:53:04 And this actually made it to a General Electric system. I don't know if it's still there, but it was actually implemented at that time. So, what are the [unintelligible], what are the things, what are the sort of things that [unintelligible] has been studying for many years? Let me give you a very, very quick overview. So, there's a - well, before I talk about this one, there are people like Brandon and [unintelligible] the people from FDA, a lot of people working on methodology, ROC, how to do evaluation.

04:53:35 There's a lot of involved statistical methods, and those are required to be able to correctly assess image quality, whether [unintelligible] is better than the other. There are a group of people, including [unintelligible], and Elizabeth Krupinski, a lot of people trying to understand so what makes



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somebody an expert. This is actually from Claudia [ph.] [unintelligible], who's now in Australia, and you can see the eye patterns of an expert and somebody who's naïve or less trained.

04:54:05 And I think we can talk later [unintelligible] which one is the expert and which one is not the expert's. So, and there's still a lot to know about what makes an expert, and we talked about that. I think vision science has a lot to contribute to try to use some of the tools from vision science to try to figure out [unintelligible] what makes an expert an expert. We don't have a full understanding. One minute. Okay.

04:54:31 So, understanding how doctors are actually using [unintelligible], you know, what [unintelligible] are they using to actually do a diagnostic [unintelligible] also involves a lot - a big [unintelligible] of actually trying to understand the statistics of the noise in the images and also doing very careful psychophysics [ph.] where you actually manipulate the statistics of the images and try to see how humans adopt - how they change their

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strategy, which features and what [unintelligible]  
they use to [unintelligible].

04:55:00 There's [unintelligible] at least 20 years of  
literature doing these sort of studies, and they have  
been tremendously useful to develop what we call -  
you've heard this word in the more complicated  
models, sort of the ones we've used in my lab for  
many years, what's called the [unintelligible]  
observer. Have you seen that term thrown around?  
That is really a model that is inspired on some  
components of human vision and its attempt is really  
to try to use those models as metrics of  
[unintelligible].

04:55:27 [unintelligible] engineers and [unintelligible] have  
pushed, you know, very basic simple methods to  
evaluate the quality of images like the variance of a  
pixel or the contrast of a pixel, things that we know  
do not correlate with [unintelligible]. You heard  
that term before, [unintelligible] and that's really  
sort of the idea behind these models. These models  
are models that are actually being [unintelligible]

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images and they're actually - they're trying to  
really model how humans do it.

04:55:56 If you want to read more about that, there's  
[unintelligible] literature on that. I think that a  
good place to look at this where it's most integrated  
within the science of imaging is this book by Harry  
Barrett and Kyle Myers [unintelligible]. A lot of  
their students have worked on [unintelligible]  
*Foundations of Image Science*. Okay. Stop. I have  
one more slide I think. Is that okay, my last slide?  
Are you going to clap? No? Okay. Okay. I was so  
scared about the clap.

04:56:24 Okay. So, [unintelligible] and people typically ask,  
you know, why is it important to understand  
radiologists [ph.], why is it to understand what  
makes an expert, and I have one slide that some of  
you have seen before that I love to show, which is  
this. And what you see there is [unintelligible].  
Oh, and I got my X axis cut off, but that's basically  
area under the ROC curve. This is a classic study by  
Craig Beam [ph.] where he had the same mammogram read  
by 110 radiologists across the U.S.

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04:56:55       And what you see is there's a lot of variability.  
And I think that we can do better than this. I think  
the idea here is really to try to come up with ways  
in which we can actually [unintelligible], hopefully  
bring them all up and reduce the variability. So,  
that's it. Thank you. [applause]

04:57:21       MALE: I'm going to start with the last graph you  
showed. So, can your observers demonstrate that  
variability? Can you model that variability?

04:57:30       MIGUEL ECKSTEIN: Can we model the variability? I  
think that's a fascinating question. I think right  
now these model observers are - until now model  
observers have been generic and are not tuned [ph.]  
to individual observers. I think that  
[unintelligible] something I have [unintelligible]  
observers that are actually tuned [ph.] to specific  
radiologists or observer and try to actually predict  
based on basic properties. So, [unintelligible] some  
of the properties of these models based on some basic  
type of experiments that you have model observer -  
observer-specific model observers.

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04:58:03        So, now I think you - even I think you would need more than that. We would have to [unintelligible] to be able to capture it, but it's an interesting question. Can we actually capture in the model observer the variability in radiologists? [unintelligible].

04:58:21        FEMALE: So, what is the model observer - what is the [inaudible] the model observer? So, for example, the trained radiologist is looking away from - I'm assuming the image on the right is the trained radiologist - looking away from all the [unintelligible] spots and kind of zooming in or concentrating on the potential tumor. So, what in the model - is it a template, a matching model? What is it doing? I mean [unintelligible] but I can't read all [inaudible].

04:58:51        MIGUEL ECKSTEIN: Yeah. There are a lot of details in there. So, the model observers are template models. They take into account [unintelligible] and the most models they have, sometimes they have some CFF [ph.] of different models of the CFF

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[unintelligible] the human observer. Sometimes they take into consideration what is the frequency component of the noise. So, they actually take that into account. And there are different models. They have a preliminary set where you actually extrapolate the features like you see there [unintelligible] channels or - so, at this point they're pretty simple, but they certainly cannot still explain this.

04:59:31 And this is part of the thing. There's a lot of room to going from these models are [unintelligible] for more basic tasks [ph.]. That's the clinical [unintelligible]. We're trying to - I mean the hope is to get model observers to basically do things more like clinical [unintelligible] where we can actually relate behavior with more of this [unintelligible] with actual - with model observer performance. Yeah. So, we're still not there. There's a lot of room for work.

04:59:59 MALE: A quick clarification too. What I think is the identifying feature of a model observer is the fact as opposed to a more general model is that it performs the task. You can give it an image, and it

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will give you a response. It literally could be another subject, if you will, in your experiment as opposed to something that predicts a threshold or takes statistical properties and gives you what would your average threshold be or something like that. These will actually take an image and give you some sort of a response.

05:00:31 MIGUEL ECKSTEIN: Right. It's not like a [unintelligible]. It's not like [unintelligible]. It's a different position and, yeah, you're getting a decision on it trial by trial.

05:00:40 FEMALE: [inaudible] to the level of [inaudible] safety, for example?

MIGUEL ECKSTEIN: Not yet. I would like to, but not yet. So, hoping on doing that.

05:00:52 MALE: [unintelligible] is really not as well modeled at this point. I think there's a lot of modeling that is trying and the field hasn't figured out which ones work for which tasks because obviously task is going to have a big element there. But the key [unintelligible] key about these models is they are

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not trained to the observations of the human. They are trained to the truth and the images and then they are fed in [unintelligible] that are based on physics or the psychophysics channels.

05:01:24 We know that the brain processes images through channels. And so it's more of a top-down where you have the ideal model given the statistics of the images and you build in some [unintelligible] from what we know about the visual system versus a bottom-up, which would take the human scores and try and regress or fit to those. So, it starts with the statistics in the problem rather than the observation in the human.

05:01:52 And if you can show a good correlation with the human results, and that's where these models have come to in these high-noise, random-background problems, we have demonstrated that they are predictive of the human performance without actually regression to human [unintelligible].



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05:02:14 MALE: So, has anyone tried the sort of biologically plausible models that are popular in the basic vision literature like starting with the [unintelligible]?

05:02:25 MIGUEL ECKSTEIN: That's exactly - so, that's what I tried in 1998. That's why I was hanging out with [unintelligible] and, you know, or '96 [ph.] or whatever when I was doing it and I [unintelligible] - people were using [unintelligible], you know, Craig started - you know, I met Craig at a conference. Was it '96, Craig? And [unintelligible] started looking at something. He started using - they were using square channels so [unintelligible] that doesn't make any sense.

05:02:49 So, that was coming from vision. So, I thought of using [unintelligible]. And then, you know, what you see there is putting on the sort of device [unintelligible] across things, things like [unintelligible] so there's, you know, [unintelligible]. There's a lot of things you can bring. I mean sort of my job in the medical image perception literature - [unintelligible] successful or not is that it's really bringing in a lot of these

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things from basic vision and putting them there. So there you can get, you know. This paper actually shows that some of these extra bells and whistles don't really add too much in your ability to predict human performance or to evaluate image quality.

05:03:23 But [unintelligible] things from basic models, you know, [unintelligible] and stuff like that. So, a lot of it is really bringing - it's constantly trying to infuse these models in the medical image perception literature with things from vision science. Craig is going to talk about using classification images to actually [unintelligible] and other things that we brought from vision science [unintelligible] hanging out I think with [unintelligible]. I was at [unintelligible] and I said, "Craig, this is the coolest thing."

05:03:54 And the next thing, you know, later he was applying this to sort of make inferences over what features or what templates doctors use are using this technique from vision science. So, unfortunately the communication is not as big as it should be [unintelligible] there are two different meanings.

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Medical image perception is a small underfunded struggling field that everything [unintelligible]. I can remember there was a meeting like that, but it was not the vision scientists 10 years ago, but it was mostly for reviewers in a study session to education them about medical image perception because vision people we can convince that these things are important, but a lot of people that are - you have people like, you know, the heroes like Andrew and all - there's a bunch of, you know, Harry Barrett and all the physicists that have really - that believe in this.

05:04:38 But I'm sure Harry Barrett and a lot of people could - and Brandon can tell us about the many people that don't, you know, that do not even know about this.

05:04:49 FEMALE: [inaudible].

05:04:56 MALE: Yeah. So, [unintelligible] now instead of us asking specific questions about the talk we've just had, let's open it up and have a little more of a general discussion. And again, please, if you

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haven't been asking questions yet, if you've been waiting for the moment, this is the moment.

05:05:24 MALE: Now is it my moment? [laughter]

05:05:34 MALE: I was going to ask about adding - we've already talked about this, but actually explicitly adding digital boredom, digital distraction, and digital blood sugar.

05:05:57 FEMALE: I have a general question about sort of this modeling from what I heard from some people over here versus Miguel is there's often the tension between trying to model the way the humans do it versus trying to model - make a system that does a really good job of diagnosis or does better than the humans. Maybe they're not going to do it the right way. And I don't have a good - and you're building a human model. Are you guys trying to build human models or are you doing it - or...?

MALE: [inaudible].

FEMALE: Yeah, that'd be great.

05:06:34 MALE: Okay. So, I would draw a distinction. So, in many of the test cases we have, you can derive an

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ideal observer and then you have to disadvantage your model in order to make it behave like a human because a human's not like an ideal observer. There's a lot of times where we're remarkably efficient relative to an ideal observer, but there's a lot of times when we aren't. When we go to medical images, you can't build an ideal observer anymore or you can't [ph.] at least arrive at some first principle.

05:07:01 Maybe you can build it by a computational learning kind of an algorithm. Perhaps people are working very hard to do that and they're struggling and they're not - there's not a clear win for a lot of computer diagnosis I would say. And so human observers may be the best thing that we've got. So, you're kind of going between these two situations. The laboratory [unintelligible] where you can build all these things, you can understand how much information is there, diagnostic information is there to be had in this image and how much are human observers taking out.

05:07:32 And then you go to the clinic where you don't really know how much diagnostic information is there. So,

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we'd like to predict what humans can get. So, the hope is by building these disadvantages in, it's not clear that they're a disadvantage when you go to the clinic anymore because the whole stimulus has changed a lot. So, there's a lot of ambiguity there and people are kind of muddling their way through as best as they can.

05:07:57 MALE: Yeah. So, to clarify, these model observers, their purpose is really as a way to rapidly evaluate technology or optimize technology or imaging without doing hundreds of studies. So, you say well, I can't do a study for like a thousand conditions with radiologists. It costs a lot of money. They don't have time. It's not possible. So, we use these model observers to evaluate things instead of things that are more crude that are known to not correlate with human performance.

05:08:23 And what Andrew presented, that virtual clinical trial, it really incorporates a model observer that actually derived from this literature. So, I'm not exaggerating. I see as having 20 years in this field, I see the model observer thing as being a sort

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of a success story because it's made it to the FDA.  
There are companies like [unintelligible] using it.  
And back in the day when I was a grad student or just  
finished, it was just a bunch of very informed  
knowledgeable guys just shouting yeah, this is  
important.

05:08:57 And so it sort of went somewhere. There's still lots  
to learn because, you know, and the imaging  
technology is changing, but I think in general it's  
great to say that it's gone somewhere. It's a good  
story.

05:09:09 MALE: Yeah. I think what you need to distinguish  
here is [unintelligible], which is CAD research is  
actually trying to do better than the human observer,  
right. Whereas, what we're trying to do is just to  
understand and predict the human observer and predict  
the performance of the human observer to the  
modalities that we're giving them, right. And so  
there's always - I mean from these [unintelligible]  
we know there's more information in the image than  
the human observer is extracting, but we don't quite

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know, you know, is there more information the human  
observer can extract? Right.

05:09:40 And so a lot of this is guiding us in our exploration  
of these things. But ultimately CAD research is sort  
of the opposite one, which is how much can we  
possibly get out. And we find even when we present  
that information to the radiologist, they often  
ignore it or it distracts them in such bad ways that  
their performance degrades. I mean the vast majority  
of the literature that has been published for CAD  
clinical use is that CAD is a distraction. All  
right.

05:10:06 And it's not supposed to be. It's just a, you know,  
when we present it to radiologist, it's, "Did you  
look here?" And the radiologist is supposed to say,  
"Yeah, it's nothing." But as soon as you go, "Did  
you look here?" the radiologist goes, "Oh, why should  
I be worried about that?" And they become more sort  
of tenuous and they have trouble making decisions and  
they start making wrong decisions, right. And so  
this is very hard. It's like I mean [unintelligible]  
did an experiment years ago when he was looking



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[unintelligible] at eye research where he said if someone - there's these areas [ph.] where people pause and fixate on a region and then something will trigger them to say no, that's not a cancer, right.

05:10:47 And even [unintelligible] said, "Why did you look here?" And they'd say, "I didn't look there." He says, "No, no, no, you looked there for like 1.2 seconds. You really fixated there." "No, I didn't." "Yeah, you did. Right there." "Oh, Jesus, a cancer there," right. And something in their eye or something very low in the visual processing system had found it and then something high had vetoed it, right. So, he designed a very simple tool, which was every time you fixated on a region for more than like a second [unintelligible] threshold, it put a little [unintelligible] there to sort of key you in that you were looking there. It drove radiologists nuts. [laughter] Their performance just tanked. You couldn't do it.

05:11:41 MALE: [unintelligible] issue with respect to actually detecting the tumors themselves. I wonder to what extent you guys have been in touch with the

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deep learning algorithms that people have been developing, computer vision, because in the last two to three years in the domain of object recognition [unintelligible] cutoff to humans. [unintelligible] as good as we are. And there's been really like a revolution. So, is there something like that that's going to happen? Do you guys know?

05:12:26 MALE: [inaudible] so far. So, in the case of [unintelligible] it has been very successful. So, one of the [unintelligible] structure activity relationship, for drug discovery. It has been used for mitosis detection [unintelligible] pathology. It has been very successful, but in general it has so far not penetrated as much into the medical field. I guess the medical field is usually several years behind.

05:13:05 So, [unintelligible] vision community really caught up with it after 2012, and the medical side is several years behind. So, hopefully soon more people will start using that. At the FDA we just actually sent the proposal to get the funding to use it for [unintelligible], but we will see how that pans out.

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But yeah, definitely it has completely changed the way people looked at these problems. A lot of problems that when I graduated seemed to be impossible to solve are now, you know, very trivial with these systems.

05:13:44 One of the experiments they had was for a test that has a thousand different object categories. So, the previous state of the arts with a lot of bells and whistles was like 26 percent correct classification or [unintelligible] error rate. With [unintelligible] it went to 15 percent. All of a sudden it just nosedived, that error rate. And then in the years since it has gone down to I think 5.5 percent.

05:14:16 So, within a few years it's going to basically go down even further [unintelligible] thousands of [unintelligible] students would have graduated [unintelligible] each one, you know, improving the result by .1 percent and now all of a sudden it's just going bam, bam, bam. It's just the feeling all those [unintelligible] problems are just going away.

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So, it shouldn't be any different in the medical domain.

05:14:41 MALE: [unintelligible] you're quoting [unintelligible] based on the [unintelligible] datasets?

MALE: We measure data.

05:14:48 MALE: So, deep learning, how many exemplars does it need? Because that's one of the real problems in medical imaging is label the exemplars.

MALE: [inaudible] you can [ph.] train on unlabeled examples [inaudible] and then you can just [inaudible].

MALE: That may prove so.

MALE: Yeah. Well, that makes a big difference because [inaudible]...

MALE: But that's also the reason why the medical world is a little bit behind too. It takes us a while to gather the cases and such. It's not just that we're slow.

05:15:21 MALE: You need large databases basically. So, if you don't [inaudible].

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05:15:24 [no audio]

05:17:54 MALE: It's a little bit - my understanding is that it's a little bit like a glass half empty, half full thing though. So, with conventional machine learning you would have a hope of trying to really quantify what the features of the target are that you're looking for, but with deep learning in some sense you're abandoning [unintelligible] understanding of what the actual features are.

05:18:20 You're saying oh well, this looks like this line has started to come into a nose or something like that, but you're not able to really trace it down to the actual low-level features anymore.

05:18:33 MALE: Well, it depends on how much you get.

[laughter] If you get [inaudible] results, I mean [inaudible]...

MALE: It's true.

MALE: ...[inaudible] because really a lot of [inaudible] multidimensional [inaudible] thinking how do you pick up the [inaudible] possible anyway.

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05:18:59 MALE: Yeah. I think it [inaudible] time to move on.

MALE: Okay. But that's an excellent point though, how much you care. Do you actually care what the features of cancer area or do you just want something that would automatically detect it?

MALE: [inaudible].

05:19:13 FEMALE: So, I just wanted to actually bring up a couple of topics that I haven't heard much discussion on today or any at all. And it's sort of what Richard just asked reminded me that it's something to bring up here. So, we've been talking a lot about standard diagnosis or having machines help with standard diagnose or CAD, et cetera, but one of the very interesting areas that's going on right now is what's being termed loosely radiomic. And I don't know how many of you are familiar with this or not.

05:19:43 But basically there are two terms, and I'll talk a little bit about both. So, radiomic and radiogenomic. So, radiomic is basically taking your standard set of chest CTs for people who have non-small-cell lung cancer. So, we already know that. But just as Richard was saying, here's a

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hundred, and what sort of imaging data beyond my ability to visually evaluate the scan is available within the [unintelligible] of the CT scan to maybe separate out good performers from poor performers?

05:20:19 So, there are several centers both in the U.S. and in Europe who are working on this, and I'm sure several other places. But some of the work, for instance, that [unintelligible] have sort of taken all the imaging data from the CT scan, so beyond your morphologic contrast, et cetera, and basically put out 80 to 100 features from this digital dataset and basically make a heat map to show which of the features actually correlated with a shorter overall survival and things of that sort.

05:20:57 And then these have been classified, and Aerts, A-E-R-T-S, I think from the Netherlands did a large dataset. And people are trying two things. One is just let the machine do all the work and see how well it does or have the machine do it first and then take four or five, you know, basically high-performing indices or the most sort of prognostic, if you will,

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which you still can't see, but you have to  
[unintelligible] extraction and see how that does.

05:21:26 So, there's a lot of exciting work going on with  
that. Non-small-cell is one they've used a lot of.  
But the radiogenomics is the other component where we  
have at NCI, and some of you may know this or not,  
but there's been a large project going on for the  
last 8 or 10 years called TCGA, which is The Cancer  
Genome Atlas. So, GBM, glioblastoma multiforme, renal  
cell cancer, breast, and a few other histologies were  
studied because of their known prominent mutation  
status.

05:22:01 So, basic standard of care going on across the  
country. But if a patient fit X, Y, and Z criteria,  
a part of their biopsy or resection was sent to these  
centers, which basically mapped out their entire  
tumor. So, what the cancer imaging program did as a  
little bit of a [unintelligible] because the standard  
of care was obtained but not the imaging. So, we  
said wait a minute, imaging is part of the standard  
of care.



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05:22:26 So, we tried [unintelligible] as possible to collect the CT or the MR at that time of the diagnosis and resection. And we have a website that you may want to visit, and it's called the TCIA, which is The Cancer Imaging Archive. And there are links to it from the Cancer Imaging Program. And basically we have large datasets of de-identified images for the people with the brain or renal cell tumor, et cetera.

05:22:57 And they have done these many groups. These are self-assembled investigators who started doing the analysis between sort of doing the radiomic extraction and trying to relate that to the genomic subspecies that were done. So, a couple of other things that you might want to talk about, but you were talking about deep learning, and there's a lot of work going on in that in radiology but as radiomic.

05:23:21 FEMALE: [inaudible].

05:23:30 MALE: TCIA, by the way, turns out to be the Tree Care Industry Association.

05:25:00

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05:26:09 Yukako Yagi: So this is the first slide. Usually we start. Yeah this is the first slide. This is a scan, [unintelligible] imaging scanner. And we scan. [unintelligible] shows how much the image, not only graphs the image, show the growth, mark growth. So this is the first diagnosis in pathology.

05:26:34 So then some of the country, developing countries. [unintelligible] scan, this is their diagnosis, is based on this. [unintelligible] they don't look at the graph size. But they had to know how to read the graph size.

05:26:51 So then this one is the specific feature that we [unintelligible] look like soft tissue. And they also like yellow to pink, on this one yellow to grey, so then this one actually pink to grey. But on the screen it kind of over this. But [unintelligible] over this.

05:27:11 So then, also histology slide we have many different. This is the image of a special stain where you look at the different [unintelligible] from each - Special stain usually we look at the more distribution and

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morphology. [unintelligible] We look at the  
morphology and also color.

05:27:32 And then immuno-stain [phonetic] like sometime we  
look at the, we count, and we also evaluate the  
intensity. Then [unintelligible] is the very tough  
part. We have to count how many [unintelligible] in  
one [unintelligible]. Some overlapping areas are very  
difficult to count.

05:27:57 So then this is the basic like histology that  
[unintelligible] entire slide, then they look at the  
raw power of them going to [unintelligible]

05:28:12 So then to make diagnosis [unintelligible] this  
slide, OK they look at [unintelligible] area. So then  
this one, it's the same thing, special stain then  
actually some time in immuno-histo-chemistry  
[phonetic] then we can combine to one stain.

05:28:32 So this one is the reusing third slide, we can use  
only one. This one actually because we moved the  
digital, we can overlap in digital but this one  
critical stain. Double stain. So then the image

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[unintelligible] we have same slide we're looking at the [unintelligible] monitor. And then totally the color sometimes different. So then, OK when we look at the image we don't know where that cause the problem.

05:29:00 Sometimes it iamge the slide has the problems, the color is totally different, looks the same, but maybe scanner was the problem. [unintelligible] maybe caused the problem. But the interesting thing [unintelligible] pathology to look up the slide in the microscope because they have the glass sliders, and they're [unintelligible] they can adjust their brain to [unintelligible] the color.

05:29:23 So even the image is not under the microscope. Many pathologists look at the yellow color. But they don't care much. But when we move to digital like when they look at the screen they don't like yellow. They want to [white]. Then some of the scanners, [unintelligible] this one material was 5% of an image [unintelligible] has like out of focus.

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05:29:50 So this is a developed focus, but the  
[unintelligible] but only one area has a little  
[unintelligible] tissue. So then the scanner couldn't  
focus. So this is a regular workflow while closing.  
This is [unintelligible] and then made the slide and  
the scanning.

05:30:09 So if we have [unintelligible] slide imaging. So we  
want to do like off color, we have to do the color  
[unintelligible] this image [unintelligible]  
variation then [unintelligible] and the digital stain  
will come.

05:30:24 So then those are the reasons we have developed in  
our lab the histology slide quality and then to  
decide how to scan it. And then this one made the  
quality variation during and after the scanning.

05:30:38 [unintelligible]

05:30:44 So that is some way to deal with the sickness of the  
tissue. So we scan multilayer. But this takes longer.  
And also the size is bigger. [unintelligible]  
Sometime we can use like [unintelligible].

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- 05:31:03        So then... Also we use in our lab with many 3-D  
meeting research, we found new finding  
[unintelligible] especially lung cancer there's  
something they didn't know before we discovered new  
area. So we're changing because - based on our  
findings we're changing classification  
[unintelligible].
- 05:31:29        So we're working with a WHO but our finding is right.  
So then this monitor, this is original image and then  
we can find the [unintelligible] And then we move  
[unintelligible] from this 3-D image.
- 05:31:43        So then we can make [unintelligible] and right now we  
count images. So then [unintelligible] Also this is  
the last slide.
- 05:31:51        So [unintelligible] modality, because many modality  
want to compare pathology diagnosis, and also the  
[unintelligible] diagnosis, other modality. So this  
one [unintelligible] and this image includes the  
entire brain tissue. But some of the tissue is  
included. So then we combine [unintelligible] and  
then MRI and the histology.

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- 05:32:18        So that case we can see a tumor more clearly. Yeah.  
So then, this we started this modality study  
[unintelligible] some of the area they look at the  
MRI they didn't know how to read it. There's some  
white area they wanted to discover [unintelligible].  
So they wanted to see [unintelligible]. Thank you.  
[applause]
- 05:32:45
- 05:32:51        Male:        So how sensitive are pathologists to changes  
in the color? I mean are they trained on these  
particular colors and if the colors are off then they  
can't interpret the image or is there some perceptual  
flexibility there?
- 05:33:08        Yukako Yagi: Yeah. It will be no [unintelligible]  
how it looks like the glass slide, they don't  
complain much. But the same with key image we don't  
have [unintelligible] glass slide in our hands. So  
that's why the pathologists are confused. So then  
some of the cases, yeah they look at the color, in  
some case color is the key to evaluate, I mean to  
make the diagnosis, the graduation, yeah so. It  
depends.

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05:33:50 Male: It's much less critical than it might be thought. And my proof for that is until the last few decades all pathology journals and textbooks were printed in black and white, true. In fact I have a slide somewhere that, covers of a textbook that's 2048 images, four in color.

05:34:12 So I think it's really a question of can you see? Is it too dark? Is it over stained? Is it under stained? Have the stains faded? Is the section too thick and therefore it's too dark? But if you have, I mean that picture there is very discolored. I mean that may be an immunoassay [phonetic] chemical stain, right?

05:34:30 [inaudible female response]

Male: Right, but even so, I mean even if that were a bad H&E you could make a diagnosis on it.

05:34:38 Yukako Yagi: Yeah. But to use for clinical like a routine basis is different.

Male: Well people have preferences, they liked it one color versus another color, but if you force they'll make the diagnosis.



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05:34:48 Yukako Yagi: I think - Yeah, but like in the [unintelligible] part, like if we give image to pathologists to make a diagnosis, actually if there's a summary, like we don't want to give [unintelligible]. But then also we know which one to correct, which one we want to show, and we want to explain the color it not so important, but the we don't know anything about the case and we have to make the diagnosis [unintelligible] same color as much as possible.

05:35:27 Male: One thing that we know very well that it might be a difference between the slides on the natural light or on the microscope, and once you take a picture and put them on the computer is that you lose the illuminant information when they're on the computer. So that we know that we're very sensitive to illuminant so we can discount them fairly well. So that, maybe that's what they're, that's what's throwing people off is that they no longer have the illuminant.

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- 05:35:54 Yukako Yagi: Yeah so actually we're doing  
[unintelligible] I'm in the pathology area, so it's  
like a calibrated monitor. So then even though light  
is adjusted. So we have, [unintelligible] If we use  
like this kind of image, like a \$20,000 dollar  
monitor is not so useful.
- 05:36:13 So we have \$100 to \$20,000 dollar difference  
[unintelligible] monitor for the pathologists to look  
at. The way we started, actually on the  
[unintelligible] other monitor they liked it. Buying  
like quick \$200, or like \$100 dollar monitor  
[unintelligible] thousand dollar monitor, but now  
like between [unintelligible].
- 05:36:43 Male: I should just point out that there are other  
fields that the color calibration is much more  
important like dermatology or endoscopy things like  
that where the color actually conveys a lot of  
information. And there, the calibration, the monitors  
is a very tricky thing to do.
- 05:36:58 And actually, I mean just from my professional point  
of view I'm the chief of physics for radiology for

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the health system. I have very little input into pathology or dermatology. These other places they do not really have the strict 2C [phonetic] that we do in radiology. They are not used to having that.

05:37:18 You know they had a light bulb. And you know it went out and they recognized it would go out. And so there's a big learning curve. We're actually involved a lot with our virtual clinical trial where Gubarko [phonetic] with defining standards for color monitors. And in fact, when the outcomes of our current grant is, Barko [phonetic] just released a new color monitor, a 12 megapixel color monitor. I know a lot of the technology that was built into that was first prototyped with VCT [phonetic].

05:37:52 Yukako Yagi: Very interesting. The model actually [unintelligible] we're using [unintelligible] microscopes. So there's 15 people look at the same microscope. But sometime more, like 20 people here, we use four monitor on the microscope. So the microscope is very little, but no one complains. But when they look at the monitors everyone starts saying [unintelligible]. So, yeah. [unintelligible]

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- 05:38:27 Exactly the same as the monitor and that microscope.  
But the pathologists they don't like.
- 05:38:33 Male: Yeah, from a radiology point of view we  
typically train side by side. And so one of our big  
concerns is the angular characteristics of the  
monitor because the radiologist attending will see  
something, point to it, and if the resident is next  
to the fellow, is next to a visiting person who is  
like "I don't see anything." And literally they can't  
because from that angle there's no contrast for that  
object.
- 05:39:00 Yukako Yagi: [unintelligible] So they want to see  
[unintelligible] in the monitor when we look at the  
project [unintelligible] monitor. But when they look  
at microscope they're ok.
- 05:39:15 [setting up next slide - no discussion]
- 05:40:12 Male: Sometimes the smart tray isn't as smart as  
it should be.
- 05:40:16 [continuing to setup]

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- 05:40:26      Male:      So Wolfe. One slide there we go. Single  
image, all right take it away.
- 05:40:37      Male: No animation, no work. [laughter]
- 05:40:46      Jeremy Wolfe: This is, this is Ed. So the ideological  
part of this, of our work is to say that when  
radiologists, or other experts are doing these sort  
of complex visual search tasks they are doing it with  
the search engine that all of us non-experts have.  
And that if you want to understand search errors, if  
you want to understand a substantial portion of the  
errors that get made in screening radiology, or  
airport screening, or whatever that the place to look  
for that is in the limits to human visual, human  
cognitive, human attentional processing.
- 05:41:31      So this is one slice through a lung, from a lung CT,  
right you'd have several hundred slices potentially  
through the lung. And what the radiologist is  
actually doing is screening, is scrolling back and  
forth looking for lung nodules. They're guiding their  
attention to round white [inaudible].

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05:41:57 And one of the questions, so a number of the things that I'm going to talk about very briefly are things that have been raised as questions during the course of the day. So there's an eye movement literature for instance on radiology images, but this was done in the days of plain film. Now so much of the search that people are doing is through volumes of image data. How do you search through that? Nobody knows. Well nobody knew. We started eye tracking.

05:42:27 What we discovered was that in doing this task there are two kinds of screeners, we call them drillers and scanners. Drillers fit typically in one quadrant and go all the way through the depth [inaudible]. So they sit in one location in XY and move in Z.

05:42:46 Scanners tend to look all over the place in XY and only move very much more slowly in Z. When you're moving in Z you tend to be wiggling back and forth. Somebody mentioned the idea of motion pop outs, that's because things that are tubed, blood vessels that are tubed in this image don't vanish and appear

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the way that nodules do. They pop in and out of  
vision.

05:43:14 So if you're modeling this salience model that  
includes motion information it's going to be more  
useful than a standard static sort of image. Somebody  
was asking earlier, "How do you learn how to do  
this?" We think that the drillers and scanners became  
drillers and scanners because they sat next to a  
driller or scanner when they were training. Not  
active, but uniformly. But that's part of it.

05:43:40 Some of you will have noticed that there's something  
a little odd about this particular light, which would  
be the gorilla in the upper right quadrant.

05:43:52 [walks away from microphone making audio very quiet]  
On the last tape of this particular [unintelligible]  
study we put a gorilla in there. 84% of our  
radiologists failed to report the gorilla.

05:44:04 Radiology once we published this in "Inside Science"  
last year, radiologists [unintelligible] with people  
complaining - Well stating either that we already

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knew that or that they would dismiss the study, the gorilla. We're very careful to point out that not that radiologists, excuse me bad radiologists who [unintelligible] or anything like that. It just points that they are working with the same search engine that you and I are working with.

05:44:32 If you are subject to inattentive blindness, which you are - sorry on the webinar. [Speaker is back in front of the microphone] If you're subject to inattentive blindness there's no reason to assume that you become immune, and there's every reason to assume that you do not become immune simply because you become a domain expert. You're still subject to the same sort of limits, inattentive blindness being just one of them.

05:45:04 Last point, it's been discussed a number of times, well the recurring theme is why don't we just get the computer to do it? Or at least why doesn't computer aid the detection help in these sorts of situations? One of the reasons for that goes back to this prevalence problem that we had talked about earlier in this meeting.



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05:45:27 Imagine that you've got a really good CAD system that detects say 90% of cancers, and false alarms on only 10% of images. Now imagine that you're doing this at low prevalence. You've got a thousand cases. There are three cancers, which is typical for breast cancer screenings, three cancer in the thousand, let's assume the CAD finds all three of them.

05:45:56 The CAD is also going to false alarm on a hundred, 10% of the cases. So now I'm delivering to the radiologist a message that's good, it has a positive predictive value, 3%. If I'm giving you advice that's good 3% of the time about who you should date, or where you should go to eat dinner, or whatever, how interested are you in that information?

05:46:17 The answer is not terribly, not terribly interested. And this may explain why, for example in one of Bob Nishakawa's [phonetic] recent studies radiologists managed to fail to act on 70% of cancers that were missed on initial screenings, picked up by the CAD on the spell check second reading, the way the CAD is

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supposed to be used. 70% of the marks on good cancers were ignored by radiologists.

05:46:47 CAD systems can be quite good, radiologists can be quite good, but there's a really important area of research here to try to figure out how to make the human and the computer work decently together. I'll stop there. [applause]

05:47:05 [inaudible female speaker in the background]

05:47:29 Jeremy Wolfe: Just because I only showed one image now you, I could show lots of relevant images...

05:47:41 Male: So, yeah Jeremy do you think - So radiologists see abnormalities in images and decide not to call them, right, that's what we call the perceptual error. Do you know if CAD, so CAD flagging those, would they have called those cancers if CAD hadn't flagged them?

05:48:03 So, you said 17% - Oh, 70 of the cancers CAD flagged they failed to act on anything that they hadn't spotted in their first read, is that right?

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05:48:15 [Jeremy talking inaudibly in background]

05:48:15 Male: No I'm asking you if there was no CAD, is CAD the problem or is it that they discount it?

05:48:23 Jeremy: Is it below their threshold for detection is I guess what I'm trying to get at. Those things that CAD found because it can afford this really horrible false positive rate because it's not making the ultimate decision, is it just finding things that are below threshold for a radiologist?

05:48:44 I don't think so. But I would defer perhaps to Brandon who might know, no Brandon is looking at me like what the hell is he talking about? [laughter] I won't defer to Brandon. I don't think that's particularly, I don't think that's particularly the problem.

05:49:01 I told some of my radiology colleagues in the face of these sort of data. I asked, so I asked their opinions about all sorts of, these sort of behavioral things all the time. Usually I get very qualified answers two days later. I asked the question, if CAD

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put up a mark, if CAD told you that something that you called a cancer was not a cancer would you change your mind? Every one of my radiologists was back in 5 minutes saying, "Not a chance! I would never declare something of mine a false alarm on the basis of CAD not finding it."

05:49:44 I think - This is a version of the sort of classic trust in automation problems. At least some of the CAD problem is that the radiologists just don't trust it. And they, the radiologists who we deal with, sort of piss and moan about the CAD, "It never does anything useful for me." Why do you use it? "I get an extra \$5 bucks a case, man." Yeah.

05:50:15 Do we want to see this -

05:50:21 Those people who are not in the vision community, may or may not know that the gorilla bear is an homage to a classic study where people miss the gorilla in a video by the way.

05:50:34 Male: So this is my version of [unintelligible] everyone satisfied?

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Male: Talk in the mic, sorry? [unintelligible] Is everyone satisfied? They saw the gorilla. Yeah look at that over there.

05:50:52 Male: Oh there it is.

Male: Other point which is here's my machine learning, trained on the first gorilla, find the second gorilla, so at least in an ideal world this could be a very useful approach.

05:51:05 Jeremy Wolfe: Yeah an ideal world where people have bad cases of gorilla. [laughter] Jay?

Male: I need help.

Jeremy Wolfe: You need help?

Male: I do.

05:51:17 Male: Some image and modalities you can change the viewpoint, like MRI you can rotate.

Jeremy Wolfe: Yeah, yeah.

Male: What does scanner versus billers do when they scan through that?

Jeremy Wolfe: No idea in terms of eye movements because the, the standard chest CT mode is just fixed

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X, Y, and Z axis's. And - We haven't done the  
experiment, and to my knowledge nobody else did.

05:51:48        Doing that in neuroradiology might be the place to  
look where they're rolling around all over the brain  
and stuff like that, but.

05:51:59        [Break Begins]

06:08:34        [Break Ends]

06:09:04        Male: And while we're doing this - all right. And  
then we'll just hit slide show, which I always screw  
up. It's that one. All right. And then we're going  
to - all right.

06:09:19        So very quickly before we get started on this  
session, can we have a quick show of hands, people  
who are interested in going to the group dinner  
tonight? Get a count. Hold your hands up until  
Donna [ph.] gets a count. Yes, it's McDonald's.

06:09:50        All right. We're good? And Alicia Toledano will  
explain why my computer is broken.

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06:10:12 Alicia Toledano: Yeah. Okay, so I hope I've set the microphone down low enough. Great. Okay. So I said earlier I do statistics, and I started getting involved in this quantitative imaging biomarkers. Okay. So this slide - this is a digital image. Get it? (Inaudible.) It is signals superimposed on noise, so this is a signal in there, okay?

06:10:34 I started with a series of zeros and ones. I generated them from independent Bernoullis. I made it super noisy. I made it as noisy as possible, so 50 percent chance you're going to get a zero, 50 percent chance you're going to get a one, and it just keeps going. And then the signal is a set of ones in a particular configuration.

06:10:54 I really made it a tough task, because I'm not going to tell the template, but if you think you've got it, keep it in your head. Okay, and it's 12 characters wide and six rows high, but it's not a block of ones 12 by six. And I even determined the placement at random.

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06:11:18 And I was really inspired by how difficult it is for readers of images to go in and look at - like they've got tons of data coming at them now. They don't know what they're looking for. I mean, what is this cancer going to look like? What is this melanoma, which is a type of cancer - what's that going to look like? What are these cells going to look like on my pathology slide? Okay.

06:11:39 So then I superimposed the signal, but to keep it super hard - so I only switched - if you had a zero, I switched it to a one, but if you were a one in the wrong spot, I left you as a one. So I left your noisy background. Okay? So are you frustrated yet, or should we keep talking about the challenge?

06:12:06 Does anybody think they have it? You think you have it, Ed? Okay. All right.

06:12:29 Okay, does anybody else see the W? Yeah, (inaudible). It's a smiley face. So it's a smiley face.



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06:12:49 Now, as humans, right, the second we saw that red color, we're fine. We're not even looking at, is it a one or a zero? We're looking at red versus black, and we can see it super easy. So this is what inspired me. I took the challenge of one slide very seriously, but I also took what we call reader burden and reader frustration very seriously.

06:13:13 So I gave you the answer. My son, one of my sons wanted me to do it with animation so it would still be a single slide, but I said no. Okay. So with digital imaging, we have these huge amounts of data. It takes real time to review. There's a push for low radiation doses, especially with the CT machines and with some of the mammos, the (inaudible) machines.

06:13:34 So that gives us increased noise. It gives us increased reliance on image processing. And my question for this workshop is how we can leverage quantitative imaging biomarkers to capitalize on our human abilities but also sort of decrease the burden of our human limitations. And I think it can be win-win.

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06:13:52 I don't think the QIBs can do detection. They're not supposed to do detection. So we still need something to do detection, whether it's a human or a CAD that we've been talking about. Somebody has to detect it. But the QIB, the quantitative imaging biomarker - it can stick a number on that finding.

06:14:12 It can tell you (inaudible). So what is this QIB? It's an object. It's saying it's measured. It's a number. It's going to show you, how is this normal biological process going? Is the tumor responding to therapy? Are things changing over time? Are things moving?

06:14:30 Is the thing that I'm seeing at this point in a patient's organs different from what's happening normally in that organ? So it takes hard work to develop them so that they can be accurate and precise, and that's where the quantitative imaging biomarker alliance is coming in. It's trying to say, you know, what words do you want to use when you're thinking about this?

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06:14:49 We heard earlier that sensitivity is used differently by a lot of people in this room, so there are special terminology that comes with this. How do we test it? How do we develop them and talk about what they can do? Classification being the hugest task.

06:15:07 And so humans are wondering, you know, do I need to note this down? I'm not going to write down that I see a gorilla, because I know you're playing a game with me, and I'm not looking for gorillas. But when you publish that I didn't see the gorilla, I'm going to send a note to the editor that says you shouldn't have picked on me for not seeing the gorilla. Right? And there's a lot of gut feeling that goes with classification.

06:15:28 So if there's a number, at least your gut is having to deal with the number, okay? It's not, do I think it's big enough to measure? It's, oh, okay, the measurement is already there, so now I already know if it's big enough. I know if it's growing. I know if it's becoming less metabolically active, if like (inaudible) are decreasing.

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- 06:15:50 I'm hoping that we can use these things to address this variation limitation, the variation within observer: having a bad mood, low blood sugar, beginning of the day. It's Friday, let me go home. I'm hoping that we can use them to address the variability between observers. And so maybe they're just another clue when you're making your perceptual classification.
- 06:16:14 Are you going to make a perceptual or not? Maybe this information from the quantitative imaging biomarker can help the radiologist or other subspecialist not make that perceptual error. And I know another big thing that we're looking at with CAD, at least, and hopefully with the QIBs as well is, as this amount of imaging data just becomes exorbitantly larger, it takes time to read them.
- 06:16:43 And you say, well, you know, yeah, it takes 30 percent longer to read a tomo - okay. But if every screening mammo is going to involve a tomo, you've got a real impact on workflow. So this is kind of an idea of, maybe it can target us on what to look at.

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06:17:02        Maybe it can target us on what we can rule out and speed up workflow, make it more efficient, speed it up without losing accuracy. So that's kind of what I'm interested in that pertains to today's topic, and I talked too long last time when I was introducing myself, so I'll not talk too long this time.

06:17:34        Male: I mean, it sounds like - there seems to be an inconsistency here. You can't complain about workload on the one hand and be distrusting of the automated system on the other. They're just trying to save you work.

06:17:48        Alicia Toledano: It is a really tough balance, you know, because people want to protect their jobs. People don't want to get sued for missing a diagnosis. Whenever I've done CAD reader studies, everyone's always told, you have to do (inaudible) second reading. You're never supposed to downgrade just based on the CAD. You're never supposed to downgrade. Never supposed to downgrade.

06:18:08        But then there's also this very real pressure from your clinical chair: Get the readings done. Get the

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readings done. Get the readings done. Get the readings done. So I don't know how doctors are going to solve that. I'm hoping that we can leverage some of that objectiveness and quantitative nature of the QIBs to help leverage that.

06:18:32 Male: Just a quick comment. Brandon here called smiley face. He didn't say where, but he said smiley face, which lets you know -

06:18:40 Alicia Toledano: Did you call smiley face because you knew it or because you know me?

06:18:42 Male: You ran the study, so -

06:18:43 Alicia Toledano: I ran it. I was just like, put a smiley face on a lot of stuff.

06:18:51 Male: That's the only thing that you would put in a whole bunch of zeroes and ones, because bars would be too obvious and (inaudible) would be too obvious. But we all know what a smiley face looks like. And I would say teach your deep learning algorithm now.

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06:19:09 Alicia Toledano: Yeah.

06:19:11 Male: I don't suggest that we spend the rest of the afternoon doing the study, but I wonder how many false alarm smiley faces there are in that stimulus.

06:19:19 Alicia Toledano: Send me a note. I'll have the computer look later. Okay, so we're done with the questions directly for me, right? And then we - okay. Good.

06:19:56 Male: You know (inaudible) you know exactly what to look for. Yeah?

06:20:29 Gregory Zelinsky: Wow, that's a pretty sharp angle. Are we good? Okay. I don't have a presentation for you, and I've also followed Todd's advice and just made this one slide, although he did divide it into quadrants, so (inaudible) I'm not breaking any rules. I'm good?

06:20:56 What I want to do is to tell you about some questions that I'm working on that might also be of interest to the National Cancer Institute and maybe say a few

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words about why I think that might be the case. As a few of you in the room know, I've been using eye movements to study how people search for things pretty much ever since shooting out of the graduate student starting gate many, many years ago.

06:21:20 Jeremy knows how many years ago that was, because you were on my certification committee. A little bit of visual search trivia for us this afternoon. My work has also dealt almost exclusively with visually complex stimuli, things like realistic scenes and these *Where's Waldo* picture books, puzzles.

06:21:47 But most commonly, these arrays of realistic objects. And I like these object arrays because they force me to confront the complexity of real-world stimuli while still maintaining some control over the experimental conditions. For the past eight or so years, the task that I've been most interested in is categorical search.

06:22:10 Searching for a target. That could be any member of an object category. And our lab has published extensively on this topic. If any of you are



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interested, I could tell you a whole lot more about effects of target typicality and categorical similarity and hierarchical levels, how all these things impact search performance.

06:22:31 But the upshot of all that work is that, even when we are given a really lousy cue, a categorical cue such as footwear, we're somehow able to use this dubious categorical information, you know - footwear could be anything - we're somehow able to use that target to guide our search.

06:22:54 And this brings me to the first point that I wanted to make as it relates to this workshop. When a radiologist is searching a mammogram for a tumor or a pathologist is searching through a bunch of slides for some cancer cell, they are not searching for a specific target like we also have our subjects do in our laboratory experiments.

06:23:17 Rather, they are searching for a target category, a cancer, and that category is every bit as lousy if not more than footwear, right? And the cancer category is nasty, not only in its consequences for a

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false alarm, but also in terms of knowing how to separate cancer features from non-cancer features in order to create a good target template.

06:23:47 In an attempt to wrap my head around how this sort of thing might even be possible, I've been sinking deeper and deeper into the murky waters of computer vision and trying to learn some of their mysterious ways, because it turns out that people in that community are also keenly interested in detecting categories of objects.

06:24:08 One currently popular method is called a bag of words. The way this works is that you first learn or build this sort of visual dictionary up here, and to do this, you take some features, maybe six features or whatever, around some key points in training images. These are obviously all from the lousy footwear category.

06:24:37 And you dump these features into the proverbial bag, hence the name for the method. (Inaudible) clustering or whatever clustering method is then performed on this bag of features, and the centers of

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each of these clusters becomes the visual vocabulary  
in this dictionary that you're trying to build.

06:25:00 The second (inaudible) deals with generating objects  
with scripters, which is something slightly  
different, and I don't know if we all appreciate the  
difference there. So again, features are extracted  
from key points and dumped into the bag, but now each  
of these visual words here are compared to a cluster  
from the dictionary that you'd learned up here.

06:25:27 These visual words are then sort of tallied into this  
bag of words histogram, where each of the bends  
corresponds to the (inaudible) dimensions of your  
dictionary, and the (inaudible) each of the bars here  
simply corresponds to how many visual words fell into  
each of these bar clusters.

06:25:51 You can think of this histogram as becoming a sort of  
descriptor for this particular shoe. Now, having  
done all this, we now have all of the ingredients  
that we kind of need to build a classifier for this  
object category.

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- 06:26:07 The way this works is that you would trade different histograms for a whole bunch of different shoes. These would become your positive samples, and you would create other different histograms for things that are not shoes, and these would become your negative samples.
- 06:26:24 And then you would feed these into SVM or your other favorite machine learning algorithm and try to find a classification boundary that separates these shoe features from everything else. And if you're successful in doing that, voila, you've just built yourself a shoe classifier.
- 06:26:41 Now of course finding positive and negative samples of shoes is a whole lot easier than finding positive and negative samples of cancer. Positive samples should be straightforward, and I would hope that the Cancer Institute maintains some sort of repository of images of what cancer actually looks like, because we really need those large databases of images.
- 06:27:06 And if that's not happening, then we really need to talk. But negative samples, however, are a little

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tricky. Not only do you need a whole lot of them,  
but they have to be good, something that we call hard  
negatives, because your classifier's only going to be  
as good as your negative samples.

06:27:27 And this brings me to the second point that I want to  
make, that it may be possible to use a radiologist's  
own eye movements as a means of collecting a really,  
really massive number of negative samples. So the  
idea here is that when a radiologist is looking for a  
tumor in a mammogram and they fixate on something,  
there was something about this little patch of pixels  
that caused their eye to move there in the first  
place.

06:28:00 There was something about those pixels that they  
thought might be cancer. But then, by virtue of the  
fact that they then break fixation and start scanning  
and searching elsewhere, they're telling you from  
that behavior that they decided it's not cancer after  
all.

06:28:17 So the point here is that this natural and repetitive  
sequence - whoops. Something (inaudible). This

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repetitive sequence of inspect-and-reject behaviors that are happening throughout all this screening is providing you - this information can be exploited and used to label a massive amount of training data that could be used to build a really good classifier.

06:28:50 So I really have to finish right now. One more minute. Okay. So putting these ideas together, my colleagues and I sort of wanted to demonstrate just how much information is available in these eye movements.

06:29:14 And what we found is that if you're actually able to decode a person's eye movements as they're searching for something to figure out what it is that they're searching for, you could actually tell what the target that they're looking for is just by analyzing where they place their fixations, what objects they place their fixations as they are searching for something.

06:29:38 And I won't get into the details, because I have to stop, but we used this bag of words method with SVM, and we trained up these two types of classifiers

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here, teddy bears and butterflies, and then we analyzed the target (inaudible) images. We analyzed the objects that they fixated the longest.

06:29:58 And then we compared the properties of those objects to these two classifiers, and we made our own sort of classification of what the target was based on distance to the SVM classification boundary.

06:30:14 And it turns out that doing this, getting back to some of the variability in observers, we were able to predict with perfect accuracy what each of our observers were searching for. Was it a bear, or was it a butterfly? A hundred percent of our observers using this method. So the upshot is, there's a whole lot of information in these eye movements.

06:30:35 And this information can be used in various ways. One way, to do the actual classification itself, and the other way in terms of labeling data - lots of opportunity here to label data with eye movements, I think. So thank you.

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06:30:55 Female: That last part - you were able to do that because you knew bears and butterflies to begin with, right? Would you be able to go from eye movements to sort of generate some sort of guess as to what they're looking for when we don't know what they're looking for?

06:31:14 (Inaudible) because we don't know what people are looking - what good clinicians do versus not-good clinicians.

06:31:20 Gregory Zelinsky: Yeah. I mean, another project that we have on the way is trying to do this on, again, a massive sort of scale. So to analyze, to try to figure out what those features are based on where the eye movements of the (inaudible) are placed.

06:31:43 And that's a slightly different question, because it's one of feature learning, and it's one that human subjects are probably no longer well-suited to do, so we're looking at this question in monkeys. So we're having monkeys search for things, a large number of categories.



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- 06:32:04      And then trying to see whether, over tens of  
                  thousands of trials, we're able to learn what their  
                  target templates are.
- 06:32:14      Male: So in these experiments, you're looking at  
                  arrays of objects on the screen. A radiologist is  
                  looking at an image that has some structure, and the  
                  pattern of eye movements is going to be driven both  
                  by that collection of informative pixels -
- 06:32:34      I'm thinking of the negative trials that you want to  
                  collect. So it's going to be driven by the  
                  informative pixels that look like something  
                  interesting, and it's also going to be driven by, I  
                  got to look here, here, and here because these are  
                  places where cancer likes to hide on me.
- 06:32:49      Gregory Zelinsky: Well, no. But those -
- 06:32:50      Male: Will that be useful as negative information  
                  also, I'm wondering, the structural information?
- 06:32:55      Gregory Zelinsky: Well, the structural information -  
                  the reason - again, we want the hard negative, so the

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fact that the negatives kind of look like cancer -  
that's a good thing, because that's going to allow us  
to build a better classifier, right?

06:33:12 Male: No, that seems straightforward. It's the, will  
your classifier be improved by the set of pixels  
around the margin where cancer likes to hide? There  
may not be anything that looks particularly cancer-  
ish there, but I'm going to stare at that spot for a  
while because I know I've got to examine that.

06:33:35 Whereas this rather large - once I become an expert,  
apparently, this rather large area, as long as  
nobody's jumping out and biting me, I can ignore.  
And I'm just wondering whether these sort of bag-of-  
words classifiers would be helped or hindered by the  
fact that the actual image you're looking at is  
structured rather than a random array.

06:33:54 Gregory Zelinsky: Look, you've got to build your  
model to accommodate what the information is out  
there, what it's ultimately intended to do. So this  
classifier out of the box probably wouldn't capture  
that information, but it's pretty trivial to just add

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in some other feature that does capture that  
information. It really would be as simple as that.

06:34:14 You know, the radiologist tends to inspect around  
these borders or these areas, so that just becomes  
another feature, right?

06:34:23 Male: I guess a different way to continue on that  
topic is, how good would you classify (inaudible) if  
you were to use the object the object that people did  
not look at? Right? Because what we saw in the  
expert eye movements were (inaudible).

06:34:44 And then they look at the place where the tumor is or  
is not, and then you actually have very (inaudible)  
data in terms of fixations. We have a lot of data in  
terms of what they tend not to even go near. And you  
actually have something similar here. So could you  
do a classification not on the item that they looked  
the most because it had, you know, the closest to the  
template, but you could actually look at the object  
that they chose not to look at because they're on the  
other side of the (inaudible)?

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06:35:11 Gregory Zelinsky: Yeah, we actually did that very early on, and the reason I don't know the numbers off the top of my head is because we found out pretty rapidly that it was pretty bad.

06:35:25 Male: I think that that's one of the critical issues, because a lot of the time they're not even looking at whole ranges of the image, right?

06:35:36 Gregory Zelinsky: Well, no. Keep in mind that, in this case, there were target (inaudible).

06:35:42 Male: No, but, you know, classifying, the expert radiologists (inaudible) -

06:35:47 Female: Yeah, if I could just add (inaudible), and maybe it's clear to everybody else, but if you look at sort of untrained people going to trained people, eye positions, what changes is, the experts are looking at very little. They have this sort of ch, ch, ch, whereas everybody else is all over. But maybe that's obvious to everybody. But I (inaudible) yeah.

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06:36:08 And that's not what would happen here, or that wasn't useful information in your model?

06:36:14 Gregory Zelinsky: So you're saying the experts - I think the slide that you're referring to before, there was an actual target there.

06:36:23 Female: No, I'm talking about the eye movement literature in medical imaging. You can look at the PET scan paths of novices or completely untrained people compared to expert pathologists or radiologists. And what changes -

06:36:39 MD: (Inaudible) same thing with chest experts. We find far fewer eye movements in the experts compared to the novices.

06:36:46 Female: Yeah. So it's what they're avoiding, the information is in what they're avoiding, which is what Alejandro was saying.

06:36:51 Gregory Zelinsky: I don't know if it's avoiding or if it's - I mean, if you think about it in terms of them having a better classifier, then -

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06:37:04 Female: Yeah, right, but there's the question of whether you could go from looking at the eye movements for information about what it is that they're using, what are the relevant features, but by the time you're looking at experts who are (inaudible) people that know what they are, they're no longer looking at those, so the information is in the negative information in the eye movement path.

06:37:22 Gregory Zelinsky: I don't think you can read that much into the fact that they're making fewer eye movements. They're just simply better able to - remember, each fixation searches a string of decision processes, and a little decision is being made at each fixation. They have a more highly tuned classifier, and they're able to discard more information at each fixation.

06:37:45 And that'll translate into fewer eye movements.

06:37:50 Male: Greg, maybe this is going back to Kathleen's [ph.] first question. These are binary classifiers, right? It's positive evidence for a category versus

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negative evidence of everything that's not a member of that category. And something like medical imaging strikes me - we were talking about this earlier today, about the fact that the search set is very kind of amorphous and could include not only things that have variable shape, but even just fundamentally different findings of categories and so on and so -

06:38:18 I was wondering if you had - maybe this is what you meant by feature learning, but I'm wondering if you've used more continuous models reaction, map out some semantic dimensions like topic models or something where you could generalize much more broadly to a broad set of objects and object categories, and whether that might be more applicable to the medical image search.

06:38:40 Gregory Zelinsky: Yeah, I think it would be. Right now we're extending this approach to - we're trying to explain those basic-level superiority effects eventually. So we're looking at relationships between superordinate, basic, and subordinate categories.

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- 06:39:04      And superordinate categories are pretty vague  
                 (inaudible).
- 06:39:08      Male: I'm not sure that you need to go to a really  
                 broad kind of single classifier like cancer or  
                 something like that as opposed to searching for a set  
                 of different categories, perhaps each one with its  
                 own classifier. We've done experiments where we had  
                 subjects searching for any of 10 or 15 completely  
                 unrelated categories.
- 06:39:36      And people can do that stuff fine, presumably, not by  
                 coming up with some hybrid, you know, teddy bear,  
                 shoe, whatever, category. They just build a  
                 classifier that looks for each one of these things  
                 and - you know, (inaudible) -
- 06:39:49      Gregory Zelinsky: I mean, I think that's exactly  
                 right. You know, once you build a hybrid classifier,  
                 that would sort of defeat the purpose. What number  
                 are we talking about? So right here, this is almost  
                 a trivial example, because there's only two, but how  
                 many of these different sort of target templates do  
                 we need on a practical level?



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06:40:17 Male: I'll give you an example. Back in the I guess early or mid-nineties - I mean, the science has advanced a lot - there was a group of people that promoted that they could have targeting systems in the Army that could detect a tank in trees, (inaudible) find tumors in a breast.

06:40:35 I mean, this was literally what they said. You probably remember who that was. And it doesn't work, right? It's not a tractable promise, not a, you know - and I look at this, and I wonder how you would do if you had a harder problem, if instead of boots and a can and stuff you had boots and feet and socks.

06:40:57 And, you know, they were all sort of very similar colors so that, you know, it was shades of skin tone, you know, shades of natural leather and beige socks. How does your classifier work in that sort of scenario?

06:41:11 Gregory Zelinsky: The performance drops off, but as we were saying before the break with these new advances in deep learning, you know, it's going to

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get really good. It's going to get really, really  
good.

06:41:23 Male: (Inaudible) find breast cancer never worked  
either.

06:41:30 Female: (Inaudible.)

06:41:40 Gregory Zelinsky: Well, that's about a nine-degree  
(inaudible).

06:41:43 Female: (Inaudible.)

06:42:01 Gregory Zelinsky: That's when they hit the button.  
Richard.

06:42:10 Male: (Inaudible) I think historically they needed to  
have a good CRR, which stands for the (inaudible)  
rejection rate, which is part of the problem. The  
other question is, what's the ground truth?  
Actually, radiologists don't make diagnoses. They  
make suggestions for future clinical follow-up.

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06:42:34 And they say suspicious for cancer and not suspicious for cancer. They almost never go out on a limb and say, this is cancer. It's BI-RADS 4 or something. And then the other sort of related question - and that's because there actually is a high diagnostic error rate on their part.

06:42:52 So they've been trained not to stick their foot out. And what they call negative is almost never biopsy-proven to be negative. It's just what they call negative, and we don't know what it is. So that's a hard thing to train on.

06:43:12 Gregory Zelinsky: What about the positive training samples? Do we have the potential to (inaudible)?

06:43:18 Male: Anything that's been called suspicious or highly suspicious gets biopsied.

06:43:23 Male: There's the Cancer Imaging Archive, which was mentioned earlier. That is actually a huge supply of images online maintained by my colleagues at NCI.

06:43:36 Male: But those are the true positives only.

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06:43:38 Male: Right. Yeah. Yeah, I mean, if you wanted to collect a bunch of negative images, that's actually an interesting -

06:43:53 Male: Well, it's not just interesting. It's essential.

06:43:55 Male: Right, I know. But it's an interesting problem, like how do you convince people that they have to start collecting these, right?

06:44:08 Male: Your negatives can't be cups and computers and chairs, right? Or your classifiers -

06:44:14 Male: No, but it -

06:44:14 Male: (Inaudible) portions of the same images.

06:44:16 Male: Exactly. Exactly.

06:44:16 Male: (Inaudible) the entire - like if the person has a cancerous tumor somewhere over here, the rest of the image is not (inaudible).

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06:44:22 Male: Not necessarily.

06:44:22 Male: Yeah, but that's going to be a -

06:44:23 Male: More likely than not (inaudible).

06:44:26 Male: Not necessarily, no.

06:44:26 Male: (Inaudible) it's a reasonably good -

06:44:35 Male: You don't necessarily know that the rest of the breast is normal. It may well be that there's (inaudible) -

06:44:46 Male: Yeah, the numbers vary, but it's something like one in six women have either multicentric or multifocal disease. It's quite high. You can't presume that. The way you would do it in mammography is, you would take films that were, say, three or four years old.

06:45:04 So if you knew today that mammogram was read negative, then last year's, the year's before are

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increasingly negative, and therefore the probability of seeing something is - but then you're looking at potentially all technology images versus modern technology images.

06:45:19 And so it becomes a very difficult problem, and getting negative images is very hard. You can have a tumor that will sit there for, you know, 10 years and then suddenly start growing, right?

06:45:33 Male: Don't we have biopsy data for false positives?

06:45:37 Male: Yes, but again, the sampling problem doesn't mean that it's truly false.

06:45:42 Male: Yeah, yeah. Of course.

06:45:45 Male: It's less (inaudible).

06:45:45 Male: But also, those are not going to be the best cases, right?

06:45:49 Male: Right.

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- 06:45:49 Male: Because they kind of look like -
- 06:45:53 Male: They are Greg's cases. They're the hard ones that look like cancer but turned out not to be, and that might actually be a useful training set for something like what Greg talked about.
- 06:46:09 Gregory Zelinsky: To be honest, this is sort of why we like VCT [ph.]. I feel like a broken record, but you know (inaudible) is, I didn't put a lesion into this breast. I generated a normal anatomy with normal ductal structure and normal (inaudible) structure and normal vasculature.
- 06:46:25 And then you can sort of say to some degree it's normal. Now, I can't completely simulate a breast. Right? I can't simulate a real breast. I can simulate something that has the physical properties of a breast and other things, but I have some limits to how closely I can simulate it, right? So I can't use it, for example, to train a CAD system, because the CAD system will learn my statistics, not a real woman's statistics.

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- 06:46:48 But I can do the other thing. I can turn it around. If I have a good trained CAD system, I can then say, well, how often do you find false positives in cases that have no lesion in them, and how often did you miss the lesions that I put in? Right? So I have some way of validating CAD systems, but not training them.
- 06:47:06 And then, to turn that around, I can then say, well, if I can fool CAD systems a lot, then, hey, I'm sort of breast-like, because then I can fool them like breasts. So there's real nuances to the thought process.
- 06:47:20 Male: At least you've got one advantage that the security people don't, which is that cancer is not deliberately trying to hide, and it's not morphing over time. Well, it may be morphing over evolutionary time, but it's not morphing over year to year.
- 06:47:38 This year's threats probably look a lot like last year's threat in the breast, which is not necessarily true in the luggage.



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06:47:46 Female: So I guess what you're trying to do here is -  
I'm sorry. This is outlier detection, right? So  
basically some trained radiologist is much better at  
detecting it as an outlier, hones in on that. So why  
wouldn't you just train normal or at least in  
(inaudible)?

06:48:04 There are a lot of studies which will (inaudible)  
data which (inaudible) said, don't enroll someone who  
has a brain tumor. All those brains, for example,  
can be used to train what can be distribution of a  
healthy (inaudible), and then everything outside of  
that is an outlier.

06:48:29 Which is exactly what your butterfly in your thing  
is. As a woman, I would go look for shoes all the  
time. Even if it isn't a shoe, I would say, oh,  
that's a shoe. Nobody asked me to look for it, but  
there it was. So it's a question of trying to train  
with your outliers. So I don't know about breast  
images, but I guess a lot -

06:48:47 Male: (Inaudible.)

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06:48:47 Female: Yes, yeah. I mean, we -

06:48:54 Male: (Inaudible.)

06:49:02 Female: All you have to do is, I mean, we model the heterogeneity, at least. And then you're going looking for a spectrum like autism? Then you have a huge thing going from zero to one, and basically you can be anywhere, healthy, because there is no special as to when you're healthy. You're just on the spectrum. So then you would just train on distribution, get a bimodal (inaudible).

06:49:22 So I guess it's just training things not even on the same image. You can try and look for stuff which you've (inaudible) and train your system to detect that outlier (inaudible).

06:49:34 Male: I think you made a logical flaw or error, because you assume that highly trained radiologists possess the ground truth, but they have the same problem in their training as a machine learning

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system does in that the ground truth is not available.

06:49:57 They're just trained that, these are the things we look for in cancer. These are the things we look for in normal. But they don't know for sure what any particular lesion is. And if you look for a diagnostic error rate in realistic, non-highly- (inaudible) situations, they're on 30 percent, which I guess is made up of sort of half not seeing the lesion and half misinterpreting the lesion.

06:50:19 So there is no truth.

06:50:23 Male: I don't understand the obsession with true ground truth, because if you can train on what a radiologist will do and you do it really well, you will now have reproduced a radiologist who does your work automatically for free. They just have the same error rate as a radiologist. You don't have any ground truth guarantees, but you have as good as the radiologist but you're saving a boatload of money guarantees.

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- 06:50:45        That's pretty good, I think. So why can't you just use radiologists' output as truth enough, truthy enough?
- 06:50:54        Female: You trust a radiologist saying that - I mean, when you go, when the person says that you have this, you have to go in for a second study, you do go in for that second study. At least in the hospital, that's the way it's done. If my chairman says you have an anomaly there, you go in. If you can replicate that anomaly - he somehow detected that anomaly.
- 06:51:13        There was a concept of truth which all radiologists know. It might not be truth, but it is a truth.
- 06:51:40        Male: (Inaudible.)
- 06:51:45        Male: I'm on yours.
- 06:51:52        Male: (Inaudible.)
- 06:52:10        Male: All right. I'm never going to beat that.

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- 06:52:11 Male: Everybody see the smiley face? All right. We can definitely postpone you (inaudible).
- 06:52:22 Male: And Abbey, you're at the top. You want the PowerPoint (inaudible) you go. All right.
- 06:52:33 Craig Abbey: Thank you, Todd. I took you seriously at the one slide and I did the basic thing, which was to turn it into a poster, so I'll try and run through this kind of quickly. I think I probably, in terms of the content, erred on the side of specificity at the expense of sensitivity, perhaps.
- 06:52:52 So I'm going to tell you a little bit about a very technical component of CT reconstruction, which is the filtering you do to do noise control. One form of this filtering is called the Shepp-Logan filtering, and actually if you know much about it you'll look at what I did and see it is a particularly aggressive form of Shepp-Logan filtering.
- 06:53:12 The reason I did it is as an example of what I like to do, which is go look at what people in vision are

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doing and try and glom onto something and bring it back to medical imaging with good effect. What you see over here are two images. This one is what I would call a ramp-filtered CT statistic.

06:53:35 And this one is (inaudible) the one next to it - I lost my (inaudible) - has now been Shepp-Logan filtered. And you're probably looking at it going, I can't tell the difference between those. And that's exactly the way I feel when a lot of CT reconstruction people show their things and say it's so much better, and I look at it - I can't see any difference.

06:53:53 Nonetheless, the noise power spectra from these are given right here, and the standard ramp-filtered version is here, and what you're seeing up here is what we're using to model anatomy. That, we sort of use the fractal power law kind of thing. It's not the same power law of natural (inaudible) because actually it's those three things they don't occlude.

06:54:12 But nonetheless, you get a different power law. Noise in CT reconstructions, if it's left alone, will

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actually have a ramp filter. It sort of goes up with spatial frequency. And our Shepp-Logan filter's a particular kind of filter, and you can see it just basically rolls that off.

06:54:32 Then, of course, it has the same thing on the target. If you're trying to find a target, you see we're using little tiny specks, which is motivated by micro complications in breast CT. But they go all the way to (inaudible), and then when you roll them off with the Shepp-Logan filter, you drop off like this.

06:54:52 If you run localization studies in which the subject is tasked with clicking on the location of the target, and if you miss by five pixels you get no credit, if you're within five pixels you get credit, you can then compare that to an optimal observer, one that incorporates all the statistical properties to do this task as well as can be done.

06:55:13 And if you do that, you'll see two things down here. The standard efficiency relative to the ideal observer goes up with Shepp-Logan filtering. That's why we do it, right? You're more able to assess that

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information in the images. That way, if you look closely, you'll see that an observer initialed C.A. instead of another observer initialed P.N. Just saying.

06:55:38 So actually, those sort of techniques come from vision science, in my opinion at least. And then the second step, we looked at classification image analysis, in this case a form of image classification analysis that's based on localization.

06:55:56 And when you do that, looking at the cases where they get it wrong, averaging the noise field where people clicked and said, "I see it right here," and they're wrong, you can, in a sense, reproduce what they're looking for. And here is an example of what you get when you do it for the ramp-filtered version versus what you get when you do it for the Shepp-Logan-filtered version.

06:56:15 I look at those, and I see two blobs with little dark circles around them. But if you plot frequency spectra of those, what you see here is the frequency response of those two classification images along



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with the ideal observer here in the lightest color of gray, and what you see is, the effect of Shepp-Logan filtering is to enhance the frequencies right here in these important mid-range spatial frequencies before dropping off.

06:56:40 And that's really what gives you the benefit. And so what I like about this is, it gives you a mechanistic understanding of image processing. People have been image-processing for years. From a rigorous ideal observer point of view, there's no reason to process an image. All the information is in the image at the start.

06:56:58 Any transformation of that image cannot grow more information. It's all there to begin with. The only reason you do that is because you're positing a reader that has limited ability to access the information in the images, and so you are processing to make the information that's there more accessible to the reader.

06:57:16 And then, if you ask image processors, "So what are the limitations in your readers?" they will blink at

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you. Most of them have no idea. And so I think this kind of analysis is a way of analyzing readers that come out of the vision world, and then when you bring it to medical imaging you can actually help people like me in medical imaging who want to know, how do we better process images for readers?

06:57:48 And then the last part of choosing this (inaudible) an example of going to vision science and bringing back something for medical imaging. This is an example of the kind of research that has traditionally, shall we say, floundered in the shoal water of NIH study sections.

06:58:06 And I think that's an important point that we should take forward here: We need to, I don't know, come to - there's an interaction with the NIH here that is going to determine how effective this meeting will be and other meetings in this area based on how this sort of work is viewed in the context of those study sections.

06:58:32 Thank you.

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06:58:40 Male: One is, I really like the fact that you can show a different subset in these images, but is there a practical difference if you look at CT scans?

06:58:53 Craig Abbey: Well, let's see. There's two ways to answer. Yeah (inaudible) this subject using non-radiological images, there is an improvement when you do the Shepp-Logan filtering.

06:59:12 I can tell you, if you try to get radiologists to read CTs that have not been (inaudible) in some way, you're going to get politely - maybe not - dismissed or whatever. You have to do that. It's expected.

06:59:28 So this is a real aspect of clinical images. They are all (inaudible) in some way.

06:59:35 Male: My second question is, this is sort of object-naive (inaudible). Anyone here familiar with (inaudible)? So what goes on - I mean, I don't know much about them, but what these guys do is, they take the standard test x-rays and electronically subtract the bone.

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- 06:59:57       And then you can see the lungs underneath.  
                  (Inaudible) targeted image process (inaudible).
- 07:00:02       Craig Abbey: But - and that's great because human  
                  observers have masking effect. But understand,  
                  that's the limit of the human observer. The  
                  information about those lungs was already in the  
                  image.
- 07:00:16       Male: Right. (Inaudible.)
- 07:00:16       Craig Abbey: Because of masking or other phenomena  
                  like that, human observers don't have great access to  
                  that. So if you understand that, it seems to me a  
                  lot of times image processing is kind of done at  
                  random. Yeah, we tried this. We tried that. We  
                  tried -
- 07:00:34       And a more directed approach in which we understand  
                  the limitations of the human observer and then try to  
                  capitalize on processing that accommodates those  
                  limitations I think is probably a smarter way to go.  
                  Yes.

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07:00:51 Male: (Inaudible.)

07:00:53 Craig Abbey: Yeah. Not huge.

07:00:55 Male: (Inaudible.)

07:00:58 Craig Abbey: Yeah, that's a very - okay, let me make one preliminary point. If you're looking closely at this access and you're looking at efficiency with respect to the ideal observer, that's 70 percent efficient and that's 80 percent efficient. Humans are very good at this particular kind of search. That's a couple degrees. It's not huge.

07:01:16 They have unlimited viewing time. They're not restricted in their viewing distance. So it's kind of radiological conditions. Radiologists have no problem with doing this and getting closer or further away. So I don't want to restrict them either. But there's not a lot of room for suboptimal search in this task, right?

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07:01:35        So this is clearly task-specific. So a couple degrees, looking for small things, but they're not so small that they're out of your visual resolution.

07:01:50        Male: So I wanted to add like a little philosophical - your little end, which I want to add to, which I think is a good point that Craig said - the support - it's been nearly impossible to get funding for grants that do basic perceptual science on diagnostic processing and how these sorts of things where you -

07:02:12        The way we basically, some of us have gotten medical image perception grants - the way we've done it is, we've stopped trying (inaudible) doing this, and we've - always have attached an engineering problem. We're trying to optimize something that has more of a clinical relevance. Then if we get funded, we end up doing all that work.

07:02:29        Plus on the side we do all this stuff, which we like to. So there is a sort of disconnect in terms of, this stuff is nearly impossible to - something that says, look, I'm just pulling this grant to understand

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the perceptual mechanisms that - that paradigm, at least in the last 15 years, has not worked.

07:02:48 It's really, you had to go around it and said, okay, I have a technology development or some kind of practical problem, and through doing that you on the side will learn things that do it a little bit underground with your grant.

07:03:02 Craig Abbey: I'm going to sort of second that. It seems like no one owns it. The medical people don't look at the perception stuff and say, oh, this is relevant to the medical problem, and the perception people, I think, see this and say, well, that's a medical problem. So no one owns it. And either you guys have to sort of get together and figuring out how to work together and say, I'll fund my quarter.

07:03:23 You fund a quarter. We'll get the cancer people to fund half or whatever. That's really critical, because it's pertinent research, and it just doesn't fit anywhere. Actually, I would like to put on - maybe if Elizabeth [ph.] is still listening, I'll put on her cap for a second.

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07:03:45 We're both trained (inaudible), so I can do this.  
You know, we put together a letter - when was it,  
five or seven years ago? An open letter to the NIH,  
the MIPS people? Remember? I remember signing that.  
It was like five or seven years ago. Basically  
stating this problem that there's a dearth of  
funding, there's a dearth of support of research.

07:04:06 I mean, not even just financial support, but  
emotional and tractable support for this sort of  
research. I don't see that it's really changed that  
much. (Inaudible) my own situation, I got funding  
through the industry academic partnership grant, you  
know, because it was Barco and Penn, you know, an  
academic and an industry partner.

07:04:30 Of 71 grants funded in that mechanism, there's one  
basic science grant and 70 products, and I have the  
one basic science grant, and that's a very tenuous  
place to be, you know?

07:04:44 Male: All right, look, you're more or less preaching  
to the converted here. But can we expound on that



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tomorrow? There's like a whole section of the agenda that's really for talking about exactly this kind of broad - you know, what kind of stuff should NIH be funding? It's exactly that kind of stuff.

07:05:08 And I think, can we bring it back a little to the science for right now?

07:05:13 Female: I have a question about - so this stuff is really cool, and it strikes me it's essentially about signal noises, you know, signal section. And at one point you said, well, we don't need to do any processing of the image. The information is all there, and you can think of that in terms of technological point of view.

07:05:35 But I'm also wondering about - in some cases, the information isn't there, or it's ambiguous. Like, again, going back to sort of how do you organize the image, how do you interpret it, it can be one of multiple ways, and that's going to require some form of processing. What are you going to do to the signal analysis (inaudible)?

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- 07:05:53      Because here, this is all sort of threshold issues  
and -
- 07:05:56      Craig Abbey: You don't have to process an image if  
you are a likelihood ratio type of observer, right?  
You're statistically optimal, and that's great. And  
transforming the image, in that case, through image  
processing of any sort doesn't improve the  
performance of that model.
- 07:06:18      Having said that, none of us are ideal observers. So  
that's where you do need it. And things like  
ambiguity and such - that factors into that, how we  
extract information. If you have an ambiguous signal  
- this is an ambiguous signal in that you don't know  
where it is, so there's a search that you go for it.
- 07:06:37      It's unambiguous in that you know pretty much the  
target. The subjects go through a fair amount of  
training and psychometric evaluations and things like  
that before I turn them loose on the classification  
image, so they know what they're looking for. But  
nonetheless, there is an ambiguity of some sort here.

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07:06:59 This is what I can produce in the lab fairly easily.  
There's other times you could imagine multiple  
targets or something like that. It could be easily  
extended. Yeah.

07:07:11 Female: (Inaudible.)

07:07:15 Male: Very, very good. So one thing I don't  
understand in how you would model it is, if you take  
an image and, for example, just invert it, just  
flipped its color space, black and white to white to  
black, you haven't changed any of the statistics, but  
our ability to read the image - it changes  
drastically.

07:07:32 What's the math behind that?

07:07:36 Craig Abbey: Well, again, you're asking me now how  
this sort of mysterious observer that we call the  
radiologist works. And, let's see - I don't know  
about contrast conversions. I know a little bit more  
from sitting in Miguel's lab meetings about  
(inaudible) inversions and things like that.

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- 07:07:56       Whereas, presumably, this grabs from grouping and organizational effects and things like that. If you contrast-invert, again, you're making a transformation of the image. In this case, you're making it in a direction that oftentimes is less informative, all right, and that's the concern.
- 07:08:13       It's very easy to actually - I can easily transform an image so that you get worse. It's transforming it so that you get better that counts. Nonetheless, it seems like counter-informative of, why is it worse and such? So the truth is, I have no answer to tell you.
- 07:08:31       There's a simple answer for this. Miguel maybe knows.
- 07:08:33       Male: Well, there are two things going on, and it's hard to separate. One is the training, right? So if you actually (inaudible) a resident from the beginning, you just made them look at inverted images, then the question is, could they be, you know, equivalent to somebody who looked at the, you know, non-contrast-reversed?

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07:08:52 But then apart from that, there's the training thing, which is, I think the bigger effect that, when you switch, you're like, you know, you have no idea what's going on. But there are also, you know, asymmetries and decrements and increments in contrast (inaudible). So that will also be - an ideal observer doesn't have that. (Inaudible) has that.

07:09:13 So it's not just a linear function in there. So that will make a difference, but I have a feeling that the biggest (inaudible) is really the training.

07:09:22 Male: All right, I think on that note it's time to move on to the next talk. Just a note on the schedule: We've decided to swap Matt Peterson's talk and Richard Levenson's talk, so Richard, you're up.

07:09:43 Richard Levenson: (Inaudible), but I didn't expect the number of slides. (Inaudible.)

07:10:09 Oh, good. Not yet. Where's starting (inaudible)?

07:10:40 Hold on. Sorry. Just thought I -

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- 07:10:52 Female: (Inaudible.)
- 07:10:57 Richard Levenson: I humbly accept. So this is my little post-Halloween slide, and I just wanted to leave it puzzling until the next slide. But I did want to point out that this has worked largely in conjunction with Edward Wasserman at the University of Iowa. Do you know - yeah?
- 07:11:19 And Elizabeth Kravinsky [ph.], and Victor [ph.] is a postdoc or I think graduate student involved. So what do I mean by that? And I think what I mean is, I'm going to propose to you a potential player in this field that is not human, not silicon, is adaptable and inexpensive and relevant.
- 07:11:40 Pretty much. So here's the problem that this classifier was confronted with. This was one of the problems. And we worked not only in histology but also in radiology, micro classifications and mammogram masses. And so here's an example. I don't mean to insult you by showing you the benign and malignant titles up there.

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07:12:00 You knew that. But this is breast pathology on the left. The four panels on the left are benign; on the right are malignant cancer. And at least we do have ground truth; all pathologists who (inaudible). So how are we going to read this? I proposed the non-human, non-silicon-based image classifier.

07:12:19 It's a pigeon. In fact, it's cohorts of four pigeons at a time, and they sit in this little box. They're fed 85 percent of their sort of comfortable feeding level, and they have to earn their extra 15 percent of corn by getting the answers right. And so basically they're confronted with these things, and they have to pick blue or yellow -

07:12:38 - and they switch size and colors so that they don't get habituated - to tell us whether they think it's cancer or not. And they get trained. How do they do? They do really well. So here is a example of - so this is 4x, low power, medium power and semi-high power, and they started at 4x with 24 normal -

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07:13:05        Actually, there were two (inaudible). But anyway, 12 normals, 12 cancers, and the other pigeons got a different 12 normals and 12 cancers, and then they were trained. And they start nicely at 50 percent accurate. They're just there by chance. And they get rewarded, and you can see over the next two weeks they climb to around 80, 85 percent accuracy.

07:13:25        Then they get switched. Then they start rotating the images so they don't get comfortable with just the particular image, and then they got switched to 10x, and you can see right away they've already generalized from the 4x to the 10x because they start at 70 percent and get up to 90 percent. And then when they switch to 20x, they start even higher because they're now experienced pathologists, and they also get up to about that.

07:13:47        And it only takes a few days. And you can see the error bars are pretty tight. So what's potentially wrong with this study? Maybe they're just being over-trained. Maybe they're image memorizers. And birds - pigeons are prodigious image memorizers.



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Thousands of images, they can memorize, and they keep the memory for years.

07:14:09 But, fortunately, they generalize to unknowns. So the light gray are the novels. And when they're at 4x, 10x and 20x, they generalize beautifully. And just to point out - I didn't go into it, but these features that they're looking at are very different at 4x and at 20x. We had a sort of discussion about that before.

07:14:29 Some of them are so low power tissue architecture in a 20x, you're actually looking the properties of the cells themselves. And the pigeons don't care. Three minutes. No problem. Micro calcs. This is what Elizabeth contributed, among - and so these are the benigns. There are no micro calcs.

07:14:48 And these are the micro calcs, and they are pretty tricky to see. No problem. It takes a little longer, and they generalize quite well, although not as well as with the pathology. This is the interesting part. These are the masses.

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07:15:06 And I found this almost impossible. The ones on the left are benign. The ones on the right are malignant. You're looking for sort of kind of, you know, spiculations and angulations as opposed to smooth, round sort of stuff down here. But honestly, there's tremendous overlap. Here's what the birds did, and now, if you notice, these aren't days.

07:15:25 These are blocks of 10 days. They're up to 80 days struggling with this. And importantly, this goes to another thing we talked about - how can you tell a good radiologist from a bad radiologist? Well, here, for the first time, they broke into two groups - the good ones and the bad ones.

07:15:42 But even more interestingly, when they went to generalization - oops. I don't have the data. They failed. They didn't generalize. They were at 50 percent. So this was a task too hard, and all the birds were doing were memorizing images. So you can break these things out. You can see what's going on now.

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07:16:01 The question is, you can then ask questions. How important is color? These are now what I call lilacs. There is no color information. They've been monochromed and just pseudo-colored purple so the birds didn't get too shocked by going to grayscale, but there is no color information here. How did they do? They did pretty well.

07:16:19 So at the top, that was their achieved success, 90 percent with no color information. And when they switched to novel, they dropped down to 75, so that meant that color was important, because if you remember early on when we went from training to test, they went from 90 to 85.

07:16:43 Here we go from 90 to 75, so that's the benefit, if you will, of color. And so what that means is, we can quantify how much each image property contributes to the classification success. And finally, we've looked at JPEG settings. And if you look at the bottom - so this is the same image, original, and then compressed a lot and then a lot more.

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07:17:08 And if you look down here, you can see that it's gotten fuzzier. The color's gotten confused. And the effect is - now these are backwards. The bars are switched. But here's the training and novel, and then at partially compressed it was training and novel, and then even more compressed it was training and way down novel.

07:17:31 So we can now measure the effects of image compression on classification. Thanks. That's it. So we are very happy. Yeah, everyone stand up. We are very happy to collaborate, especially if someone will pay for it, and I think that for a lot of novel instrumentation or novel technology assessments, is A better than D, we can do this for pennies on the dollar.

07:18:05 Female: So back to training, so these pigeons are great. Would this be -

07:18:10 Richard Levenson: These are off-the-street pigeons.

07:18:11 Female: Exactly, yeah. And they actually are. So would a radiologist be trained this way, where they

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get trial by - not pecking and (inaudible), but these pigeons are getting reinforced on a trial-by-trial basis, albeit on a schedule.

07:18:30 Richard Levenson: I'm sorry. They're getting what?

07:18:31 Female: Reinforced.

07:18:33 Richard Levenson: Well, I think radiologists get reinforced.

07:18:34 Female: But that's my question. Really, on a trial-by-trial - do they get - I mean -

07:18:38 Richard Levenson: Well, residents don't sign out cases. They have to show their cases to their attending, and we've been considering the attending as ground truth. So, I mean, they are trained. It's not exactly the same. I mean, radiologists use words sometimes.

07:18:55 Female: Then they could be really good, like these pigeons.

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- 07:18:59 Richard Levenson: Exactly.
- 07:18:59 Female: I mean, I guess that's - but are they at that level?
- 07:19:03 Richard Levenson: Well, no. I mean, the pigeons have a much easier task than the radiologists because they're just being given salient regions of interest. They don't have to do the search before the classification. So don't rush out (inaudible).
- 07:19:17 Female: Right. But behind my question is, how good of a model for a resident having been trained to do this task is this pigeon model, given the way the training occurred and given the (inaudible)?
- 07:19:32 Richard Levenson: I mean, I think you could do it. In other words, if you could give the radiologists exactly the same images in the same way as you give the pigeons, actually, the mammograms and the micro calcs were actually shown to radiologists, and there are scores involved, but I think they were shown the whole radiogram rather than just a region.

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- 07:19:56        And there was differences. I didn't see a correlation between what the radiologists found difficult and what the pigeons found difficult.
- 07:20:04        Male: Forget residents. What about undergraduates?
- 07:20:06        Richard Levenson: Actually, a high school student, I have now who is grabbing more images for me, and she's really good at cancer versus non-cancer in breast. This is not hard. You just have to overcome your sort of fear. Also, the task is easy. It's frank cancer versus frank normal, whereas anybody can do that. Even me.
- 07:20:26        But what's hard is understanding all of the mimics, the gradients, the intermediate disease and staying alert enough to actually see it when it's in front of you.
- 07:20:36        Male: So is the suggestion to develop technology, evaluate technology, or to replace radiologists?
- 07:20:44        Richard Levenson: No.

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- 07:20:45 Male: What is the suggestion?
- 07:20:45 Richard Levenson: I would like to say that we can do flock sourcing and do the diagnostic stuff. I think you might imagine these as a prescreen.
- 07:20:55 Male: But do we have to have a relationship? If it's going to be used by radiologists, we need to then know what the relationship between the visual system of the pigeon and the visual system -
- 07:21:01 Richard Levenson: Well, it's actually very similar, and I think my point, which I sort of buried here, is that the paths that I found easy-ish, like the pathology and the micro calcs, I mean, I could see that, and pigeons, of course, are all about pecking little tiny features because that's where their food is.
- 07:21:21 They did that well. I can do that well. The masses, I found really hard and they found really hard, so, you know, it's not a big study set, but I've got a feeling that their visual system, their performance



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is, at least so far, analogous to human in a useful way.

07:21:42 Male: So I think following up on Miguel's question is whether the pigeons are doing classification in a qualitatively different way than the radiologists, and I think I'm wondering how would you know? How much have you quantified the pecking behavior?

07:22:01 Richard Levenson: Well, you can quantify a lot. You can quantify where they peck. You can also look for the latency of how long they think about it before they peck. There's all kinds of stuff that we haven't even pulled out.

07:22:10 Male: You haven't done that yet?

07:22:11 Richard Levenson: No.

07:22:11 Male: So I was going to ask you whether there's like agreement between the pigeon pecks on the benign slides and the fixations of the radiologists?

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07:22:21 Richard Levenson: We can see where they peck. But the thing is, their target is the bars, so I'm not quite sure - I think they peck on the thing, and then they peck the bar. But I'm not quite sure. I haven't seen them in action.

07:22:32 Male: Or (inaudible) for training, but you -

07:22:33 Richard Levenson: You could do that.

07:22:38 Male: If I understand correctly, in this case, if you gave these images to a pathology resident, so your uncompressed, your 30 percent and your 10 percent, what would you expect their performance to be?

07:22:53 Male: No problem. They would be at 100 percent. And this is what happens commonly, is that we see performance differences in our model system, but the question is, does it discriminate the effect correctly? And so the thing you have to be worried about is if you've encountered some sort of interaction, something whereby the human observer doesn't see this as a degradation and the pigeon does or something along those lines.

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- 07:23:18      And that's been a bugaboo for model observers.
- 07:23:24      Richard Levenson: But what I didn't show you is that  
- and we're not quite sure how well it maps yet - but  
when they were first confronted with the  
compressions, they did poorly, and over the next few  
days they did better. In other words, they say, oh,  
this doesn't bother me anymore. So there is kind of  
a habituation to these artifacts, which humans will  
do as well.
- 07:23:45      So I think that's a strength over sort of inflexible  
ideal observers, is they can kind of respond and  
relax, whereas a computer can't at the moment.
- 07:23:57      Female: Yeah, I hazard that (inaudible) we are  
discussing this as a possibility, we thought maybe  
that (inaudible) systems, but (inaudible).
- 07:24:16      Richard Levenson: Yeah. Well, I don't know if it's  
4,000. I mean, we're at 85 percent, and that's the  
average accuracy. I was asking Victor if he could  
quickly see what happens to the accuracy if you

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voted. There are four pigeons in the cohort. What if there was just three out of four? Were we up to near 100 percent? And just guessing, I would think yes.

07:24:48 But he hasn't written back to me. So, I mean, these are early, early days, and I would be delighted to have serious collaborative discussions with anyone who's interested.

07:25:04 Yep, general discussion.

07:25:15 Male: So moving to the general discussion, one thing that I'd like to hear about is the relationship between the sorts of computer vision approaches that Greg was talking about and the model observers, the numerical observers, because it sounded to me like the model observer's using a template-based system, and that seems sort of incompatible with the computer vision approach.

07:25:46 And what's the relationship between those approaches and quantitative imaging biomarkers? How do we relate these different approaches?

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- 07:26:13 Female: Okay, so it could involve administering contrast and then measuring - because of course you have to do that in things like (inaudible). Otherwise you can't know how fast the tumor eats the sugar, right? So you can have contrast, but our definition is that it's an objective characteristic derived from an (inaudible) image.
- 07:26:35 It has to be measured on a ratio or interval scale, and that's it. I mean, yeah.
- 07:26:47 Male: Greg, tell me, could you envision your search model if you really wanted to loosely define the template and say, if you do a clustering analysis, and you say, well, the centers of those clusters are templates - let's just call those templates. And so now you have a multiple-template model -
- 07:27:09 I mean, I think the real importance of those things are in the details of how - so I find distinctions of a template or non-template are less meaningful to me than actually seeing the entire model spelled out. And so by calling those templates, I don't think that

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in any way degrades the search model you're doing or  
denigrates the search model you're doing.

07:27:33 I just think that it really is in the little tiny  
details of how you actually go about saying, these  
things are a cluster, and these things are not, or,  
these things are inside what I'm calling the cluster  
of objects that I'm looking for, and these things are  
outside it.

07:27:51 Am I saying anything that seems wrong to you if I say  
that?

07:27:56 Gregory Zelinsky: No, but I sort of had the same  
questions as Todd. It depends on - your question is  
essentially about specificity, right? So with what  
degree of specificity are you treating your  
templates? I don't know what -

07:28:17 We started off today talking about, you know, is  
cancer a unitary category? Is it multiple  
categories? I think it's pretty clear that there's  
multiple categories, but there's not that many. And

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so how specific within each category - how specific  
can it be? How much variability is there?

07:28:36 We need some (inaudible), and this will bring it back  
to, you know, quantifying the variability in the  
positive samples.

07:28:46 Male: It seems to me the difference between the  
templates and the bag of words is that one of them is  
doing some series of convolutions over an image to  
actually detect regions that might contain a thing  
and then perhaps classify it, and then what you're  
doing is, you have already a segmented portion of an  
image, and you can extract features from that to  
classify it.

07:29:07 So in one case, it's doing a search. In the other  
case, it's doing classification. What you're  
treating as features into your bag of words are  
essentially the kinds of things that are being  
involved with an image to detect something in the  
observers.

07:29:21 Gregory Zelinsky: Yeah, but I think (inaudible) -

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- 07:29:22 Male: (Inaudible) same thing (inaudible).
- 07:29:24 Gregory Zelinsky: (Inaudible) some important steps, though, with regard to the specificity question. So, I mean, the features in the ideal observer - they're really just (inaudible), right?
- 07:29:37 Male: An ideal observer (inaudible) - those are human (inaudible), right? Humans have (inaudible) front end. Ideal observer (inaudible) the image.
- 07:29:48 Male: The image - it doesn't have a visual cortex. It knows the statistics of the image, and it operates on that. You could arguably say it acts on the file, right? It (inaudible) input a file and not necessarily an image. All right, so, well, that's one of the problems with it.
- 07:30:08 And so when you go to actually do these things, you try to figure out how to reduce dimensions, and there oftentimes are tricky ways to do that. Arguably, that's kind of what you're doing with all those clusters of features.



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07:30:25        So there's similarities there. So the question about the models is, how do you blink up different parts? They're kind of oftentimes big, complex models that oftentimes you could maybe make connections between them different ways.

07:30:43        Gregory Zelinsky: Well, I think one relevant dimension here is generalizability. So the whole purpose of these type of models in computer vision is that they will generalize to different conditions.

07:31:02        You're looking at a very, very limited task. True. True.

07:31:06        Male: And if you want to satisfy a medical imaging problem, you have to delve into that (inaudible) the minutiae. When I think about all the CAD developers out there, you can spend your whole career on finding these in livers, and that's what it takes, versus the generic classifier approach that will never succeed in all these different tasks.

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- 07:31:30 They really have to funnel down to the features of that (inaudible).
- 07:31:37 Gregory Zelinsky: So I think, in answer, Ben [ph.], to your question, I think that once you identify the relevant subclasses and include enough training examples, then the computer visual approach will start to approximate the ideal observer approach. But once you add in the generalization dimension, then they become less comparable in that regard.
- 07:32:00 Male: Yeah, and they're for very different purposes. That's the thing. I don't see these as competing models in any way. What Greg's proposing is to actually solve, how do we do this as best as possible with a computer? The ideal observer is where we know what the answer is, right? We've already said, let's pretend we know the answer, and now let's see what limitations we find in human observers.
- 07:32:21 So that's a different purpose than what he's going for. So in a sense, I feel like the ideal observer, when you can calculate it, that fulfills this role. Now, if we could, you know, generate full probability

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distributions of cancers and non-cancers (inaudible),  
we could generate an ideal observer for that.

07:32:43 But we'll never get there.

07:32:44 Male: (Inaudible.)

07:32:44 Male: What's that?

07:32:45 Male: You'll never do that.

07:32:46 Male: Right. And so we're left with basically a  
bunch of shortcuts to try and get us those. Some of  
those may be better than others. Maybe the deep  
learning shortcuts have finally gotten there faster  
than a lot of other approaches that have been tried  
in the past.

07:33:05 Male: But also, Greg's stuff could be also used - I  
mean, there's another valid - which I think Todd  
asked, which is another valid point, is, I mean,  
there is how to assemble the computer vision set of  
approaches, as sort of Greg mentioned. How to

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(inaudible) develop the model observer that  
incorporated those?

07:33:27 How would that compare with the set of model  
observers that we have now, with, you know, the long  
list of model observers that we have now? Because we  
have all different versions, the different channels.  
It's like, you know, there are lots of (inaudible).  
So I think that's an interesting question, whether  
you incorporate some of these things; will it buy you  
something? Will it be the same?

07:33:49 I mean, I think, you know -

07:33:52 Male: My guess would be in the subdomain they'll do  
great, and in other domains they may struggle  
depending on whether the critical assumptions behind,  
you know, the dimensionality reduction or the  
critical - are good assumptions that are safe to make  
for that particular application or not. And if  
they're not, then you need to find other ones that  
would do it.

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07:34:11 And maybe the same combination will apply, or maybe it's some sort of different way of combining features. But you might discover that, here's a combination rule that works. You just need to change the features going from liver to breast or something, or you may find that, no, you actually have to change the features you use and you have to change the way you combine them.

07:34:34 Male: (Inaudible.) I think to some degree we can draw an analogy back to the CAD software again. If you look at like - I've spoken with Julia Marshall [ph.], who's at (inaudible). Their biggest asset is their database of images, and they have hundreds of thousands of images.

07:34:53 And with that, they've gotten CAD systems. I'll get the numbers on the order of magnitude right. I might get the exact numbers wrong. So this is not a advertisement or anything for (inaudible). But for classifications, they have a sensitivity rate of like 99.98 percent or something like that, but their false positive rate can be like one every two images.

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07:35:15 Her math is, their sensitivity rate's like 80 percent with a false positive rate of one or two per image. You know, and that's with hundreds of thousands of images of training sets, all right? Just sort of general training and matching is not going to work.

07:35:37 Male: (Inaudible?)

07:35:38 Male: They won't tell us that, but it's a very large set of features, a very large set of features.

07:35:43 Male: So the training seems to be an important issue that keeps coming up over and over again, and I think it's also highlighted by Richard's presentation. One issue that was in the back of my mind putting this workshop together is, what do we know about perceptual learning that we can really apply to improving the performance of human observers?

07:36:12 And to what extent, if any, is any of that already incorporated into how they're trained?

07:36:18 Male: Well, one thing I was going to say on this front is that insofar as you think about the

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different subclasses that Greg's referring to as categories of, you know, tumors or, you know, other image artifacts, you know, I think we could draw in the category of learning literature - there's a extensive category of learning literature.

07:36:36 Yeah. And, you know, one of the classic findings in that literature, back to Posner and Keele, like 1970 or '69, is that variability during training leads to worse learning but better generalization. And so that's a very simple heuristic. If you want to train a radiologist, to have highly variable training sets will lead to better general decisions.

07:36:57 I don't know if that's part of radiological training or not, but -

07:37:01 Male: (Inaudible.)

07:37:03 Male: What's that?

07:37:04 Male: (Inaudible.) So you get what comes through the door, you know. And that's pretty variable.

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07:37:13 Male: Which is stupid, because nowadays the images are digital. You could have an amazing training set. Who cares if it was imaged today or a year ago.

07:37:21 Male: But, I mean, we've had that forever. I mean, we have great textbooks with all these sort of esoteric cases, and, you know, they study them and study them and study them.

07:37:29 Male: Just to follow up on that point, though, the best way to do category learning is not by studying. It's by trial and error, having to make a forced choice about the category membership and then getting feedback. It's mostly implicit learning, feedback-based implicit learning, as opposed to studying, reinforcement. Yeah.

07:37:46 Male: But, I mean, that's the way a lot of these texts essentially run. They actually do the cases, and then you have to sort of figure it out, and then you get it back, and you look it up, and, you know, (inaudible).

07:37:56 Male: Cool.



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07:37:58 Male: Another thing that we know from (inaudible) learning is that interspersing very good examples during training phase really (inaudible) template and accelerates learning very much. And even for finding new threshold signals, every now and then, presenting a threshold that is clearly above your threshold primes the awareness of the things that are near the threshold.

07:38:30 So those are things that can really be introduced into it. But I don't know if that's (inaudible).

07:38:38 Male: Also, people should get good sleep after every training set.

07:38:45 Male: I would say part of the problem is, we don't have ways of grading the toughness of these things. We don't know that this is easy and hard. I mean, to some degree we do, but we don't have a really fine scale for saying, this one's perceptually harder. Train on these ones this week because these are the 40 percent toughness ones, and then next week train on the 50 percent toughness ones.

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07:39:02 Male: Yeah, no, but presumably what you have is some set of images that are obvious examples, like (inaudible) like these are (inaudible). I was insulted. So I think there must be very clear cases of different types of cancer, and if you intersperse those into the set when people are learning, it will help them even make sense of the tough cases.

07:39:37 Because you precisely don't want to block them by a level of difficulty. You want to intersperse them. But also, always include - keep reminding them of what a good example is, and that helps them tune.

07:39:54 Male: In the context of mammography, I can actually (inaudible) that strategy - I understand the science behind it - actually making things difficult for radiologists (inaudible), because if you train them to say BI-RADS Category 6, it's very obvious, you know, (inaudible) kind of malignancy.

07:40:17 But then the most error-prone categories are 3 and 4, and usually those are the ones that are referred for biopsies (inaudible). And if you look at the images,

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learning from Category 6 BI-RADS images, obvious cases, is not really that much of a help in deciding what to do Category 4. So what would be (inaudible)?

07:40:46 Male: Well, I would say that that's an empirical question, because in perception, it does seem to matter when you do these perceptual learning trials. What we do is that we put a tiny signal in the periphery, then a tinier (inaudible) detection in the field of textures, and every now and then present them something that's obviously 90 degrees.

07:41:11 You think that's so obvious. How is that ever going to help people make the distinction between 10 degrees and 15 degrees? Well, it turns out that it does, and it helps huge. Every now and then you remind the visual signal, by the way, this is really inclined. All the time, it makes the 10/15 degrees information much easier.

07:41:29 So I would say that that's maybe an empirical question.

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- 07:41:32 Male: But it's been addressed. There's a group in Sydney that inserted cases much like Jeremy did, inserted obvious cases in the clinical practice. They found when they inserted obvious cases, radiologists didn't detect anything else. Performance went down. The reason why - there's a reason why. It's because of prevalence.
- 07:41:50 If you're a radiologist, you're expecting to see five out of 1,000. You see an obvious one, you see another obvious one, you're done for the day, you know? You maybe would have to tell them, we're going to insert some obvious ones or something. But that straightforward manipulation - and this, I think, is an important thing that I want people in vision to understand.
- 07:42:11 Things sometimes go awry when you go - I mean, it's a good idea. It has a great rationale behind it. The first people who implemented it got exactly the wrong results, but maybe they made a mistake or something like that. But it's very easy to go awry in those (inaudible).

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07:42:26 Male: One of things is the level at which this is implemented, right? If you're talking about implementing with experts, so prevalence is already a problem for them. But we're talking about implementing it during learning, as a training tool, and I think that's a very different - or maybe not.

07:42:44 Male: So I tried something about 10 years ago. We actually (inaudible) down the road to start a company where we would gather these cases, and then we would seed them into the workflow. And what we would do then is give them CME credit. So after that case came up, they had to be told, okay, you did just did a training case. You missed this cancer. It's right here.

07:43:06 And the reception of that was zero. They did not want that in their clinical environment. They could, you know, see how their chairman could use it against them. You know, they could see 100 negatives to this, and we couldn't move it at all.

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- 07:43:21 I've been trying to work that up for several years and never gotten any traction either, but I'm interested that you -
- 07:43:31 Male: Sounds like a top-down mandation (inaudible). No one's going to ask for it. But -
- 07:43:35 Male: But back to the distinction between the low-prevalence version and the high-prevalence version - we did a version of this not with radiologists but in the lab, but we weren't trying to do perceptual learning. We were trying to counteract prevalence effects.
- 07:43:55 And what we did was to have a high-prevalence sort of booster shot clearly identified in the middle of the normal run of low-prevalence trials. And what we found was that there we could move, in this case, their decision criterion during the low-prevalence period, but we were distinguishing between a high-prevalence training set and the low-prevalence practice.

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07:44:23       And I wonder whether or not in the perceptual learning set you might get the Alejandro results, you know, even in people who are expecting low-prevalence if you tell them, here, let's just do a few easy ones for a while, or, you know, do a high-prevalence block for a while.

07:44:40       Male: In the U.K. they'll have (inaudible) in the U.K. where you go take a test set, and they'll give you feedback as to how you've done, and they feel that that's been very successful, but that's much more - the radiologist does it. It's confidential to the radiologist. It's at their own - they're not using it, I don't believe, to do any sort of discrimination other than to train them.

07:45:06       They've done the same thing in Australia, but the Australian group has also looked at evaluating radiologists at conferences or something. You read a batch of 50 or 60 of them, and they give performance back to the radiologist, and it's something those people take very, very seriously, and they're a little bit crestfallen if they don't perform well.

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- 07:45:26        That affects their self-image and things like that.  
So it's a landscape that you have to be aware of,  
(inaudible), you know, this is how people are going  
to react in that area.
- 07:45:40        Male: I'll maybe take just a slightly different tack,  
if I could. What we haven't talked about is the  
general radiologists. You know, we haven't  
(inaudible) general radiologists. They read  
everything. And if I draw an analogy with the CAD  
systems - we don't have general CAD systems.
- 07:45:57        We don't have anything that you could just sort of  
throw any image at and it goes, oh, okay, well this  
is a chest image. I know these (inaudible) got to  
diagnose, and I have these algorithms or whatever.  
If we (inaudible) from this perceptual learning or  
any of this work, can we think towards having a  
general observer or a general CAD system or, you  
know, a generalized radiologist that can look at any  
image and have some hope of doing something with it?
- 07:46:22        Male: So perceptual learning's actually a bad model  
for general performance. Perceptual learning is



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notoriously specific except under very limited conditions. So, you know, if you train on orientation at some location in space, you get better at perceiving orientation at that location in space.

07:46:40 I think probably a more generalized performer would be more likely category learning with a broad, high-variance training set, and in perceptual learning you actually do get more general benefits if you simultaneously train on two dimensions, so if you're trained to perceive, you know, two orientations at different locations or motion and orientation at the same time interweaved.

07:47:05 So that may be the only lesson there, would be how you interweave training, so that goes back to Alejandro's point. And so I detect that there's some issues with implementing that practice. But perceptual learning itself is highly specific, unfortunately.

07:47:18 Male: Well, there's no - sorry. I have, basically, a response to that, which is that you may call it a single program, but if you imagine this idealized

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general radiology tool, you would simply have modules for each category, obviously. But yeah, the lung module would not be the same as the bone module.

07:47:39 But I'm thinking we were back to the prevalence issue and the Pap smear issue, which is, I propose maybe that we think about CAD not as computer-aided diagnosis but computer-aided discarding, where you can discard the normal and then really enrich the set that the radiologist has to look at.

07:48:00 Male: You know, that's been talked about for years, but I thought that was a slam dunk. That, I thought, was going to be the first thing we were going to see, is computer triage algorithms. And the guy from the FDA's still here, and I can't comment about anything in submission, but has anything been approved that you know of?

07:48:23 Male: I know Martin [ph.] (inaudible).

07:48:25 Female: Martin's been working on that for at least 10 years, if not longer, so we've talked about things like, yeah, it could really help radiologists focus

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on the cases that they need to spend time on, but the uptake by mammographers at least has just been, no, because if I discard it based on the CAD and I'm wrong -

07:48:48 And there you go right back to the lawsuits. So he's actually thinking there's a better chance of acceptance in a place like Canada, which is less litigious than here in the U.S.

07:48:59 Male: All right. So I think on that note, it's time to bring the discussion to a halt. We have a bunch of great talks lined up tomorrow morning. We'll be back in this room at nine a.m. And after the talks, then there is some time reserved for sort of general thoughts about the direction the field should go, the sort of discussion that we were having that I cut off earlier about complaints about what the NIH is doing.

07:49:29 That would be very welcome. But also scientific thoughts about what kind of work is not being done. So start thinking about those sort of summary things overnight. In the meantime, we've got dinner reservations at Black's, which is in Bethesda. It's

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really good. I've been there before, and they have  
good drinks. There are directions on the table back  
there.

07:49:50 We have taxis for the travelers. We have taxis  
waiting out front to take you to your hotels. The  
reservation is for 6:30. It's in my name. And  
Yukako, there's a taxi waiting to take you to the  
airport.

07:50:07 So I think that is all. I think that concludes all  
my announcements. (Inaudible) thank everybody for  
this great discussion today. Alejandro.

07:50:24

END FILE

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