So my talk will be initially to look at OCT for glaucoma detection, so we’re going to shift gears, get away from all that retina stuff, all the fancy stuff. Now we are going to talk about the real world, the trenches of glaucoma. And so I’ll start looking at you know where we are, you know both historically with some older OCT technology as well as you know where some of the newer OCT machines work in our clinical practice. And I’ll pretty much leave it at that, because the second part after Dr. Schuman’s talk is we’ll have – later on we’ll have some glaucoma cases. And I think that will really help us, we’ll have a little bit of interplay and that will help us you know really go over kind of the nuts and bolts of how we see these things and how we use this on a clinical practice. So I’ll just start setting it up you know looking at some studies, you know what, what the, the peer reviewed information is on this topic, and then we’ll shift gears a little bit and make it more practical. So I think we’ll save the cases for probably after, after your talk too, and I’m sure you have some cases in there, Dr. Schuman, as well. He has all the fancy stuff.

Okay. So really you know OCT and glaucoma, and we’ve heard a lot of this you know today is really a tool, it really doesn’t eliminate anything else that we do in our clinical taking care of patients, you know it gives us another option, it’s an adjunct to what we already do. It doesn’t replace doing functional tests like visual fields, it doesn’t obviate the need to check you know central corneal thickness, doesn’t take away having to examine the optic nerve, it’s really just another tool, but it’s a very powerful tool and it’s largely changed the way we diagnose and screen patients for glaucoma. It’s really useful for correlating to functional testing, visual field testing. You know back when I was in residency training you had to, you looked at the optic nerve, you did a visual field and you tried to
make your best guess and, and that’s kind of where you went. Now we have a lot of information and when it correlates it gives us a lot of confidence in our decision making, so we can act quicker to make therapeutic decisions, whether it’s to advance therapy or to say okay, you are somebody who is okay that we can watch.

It really helps as a nice adjunct to our optic nerve findings, we’re all ophthalmologists, we look at optic nerves every day. Some optic nerves are relatively easy to interpret, other optic nerves are virtually impossible to interpret in basically saying okay, yes, this is a glaucoma, this optic nerve this is not. And so it’s nice to have an additional tool that really can serve as an adjunct and give us different information, supporting information, similar information to what we get from our clinical exam, but it’s also different in a lot of ways in the view that it gives us.

And it also helps us to formalize areas of focal abnormalities, whether it’s a notch on the optic nerve, a defect in the nerve fiber layer, if we are fortunate enough to see that. These can be relatively typical to see these things clinically, but it helps confirm, we say okay this looks a little funny, oh here is the defect on OCT, this is giving me confidence that we’re going to go this way.

The nerve fiber layer I think is really the examination. We won’t go into studies you know looking at other parts, you know looking at the optic nerve, looking at the macula for glaucoma, all of these things have been proven to correlate pretty well, but really I think the mainstay is how it’s shaking out as we really look at the nerve fiber layer exam and that’s based on studies, you know, that have supported the hypothesis that you are going to see changes in the retinal nerve fiber layer faster or
earlier than you are going to see in the optic nerve in many patients. A lot of times it’s simultaneous, sometimes it’s easier to see changes in the optic nerve but really we are looking at the nerve fiber layer and probably in the future we’ll be looking at other structures, the retinal ganglion cell layer, etc. once we gain more information.

So you know a lot of our patients come in, they have a strange looking optic nerve, or it looks different than average or different between the two eyes, glaucoma suspects is those, it helps us sort it out. Maybe it’s just a big optic nerve compared to the other one. Family history, glaucoma suspects, we see abnormalities we are more likely to treat those patients or diagnose them. Patients with normal visual fields, we have this dilemma all the time, wow, you have really strange looking optic nerves, they look glaucomatous to me, but I can’t prove it, your visual fields are still normal. If there is some information, you know many of these patients we’ve gone and decided to treat based on changes that we’ve seen on their OCT exams, and these are you know the term we use now is pre-parametric glaucoma, before it’s showing up on a standard white on white perimetry. And we’ve seen this in studies that support this, that you know thinner OCT nerve fiber layer findings are a predictor of glaucoma.

So in clinical practice what are we doing? So we want to – we see the patient for the first time, one of the question is, is this a glaucoma patient or is this not? And so we get – we gather information on the baseline. The baseline exam has kind of two purposes, one to serve as a comparison point for the future, but also and probably more importantly in that initial exam is comparison to the population at large, kind of we are looking at you know other people who have similar demographic
characteristics, age characteristics, racial characteristics and how does this person fit into that spectrum? If they are an outlier do we have a reason that they are outlier, is glaucoma one of the reasons that they are an outlier? Or is it just you know the way, the way that they are made. So we want to get baseline exam, using normative databases is very helpful for this to say okay, where do they fit into the normative database? And if they are abnormal that’s going to push us in the direction that it’s likely that they may have glaucoma, if they are an outlier in the normative database.

But sometimes that works out well, sometimes that not. Many patients we get an abnormal test finding, first exam doesn’t really correlate to the rest of their exam and so what we’ll choose to do is follow them closely. And this is where using the follow-up exam is really using that person as their own control is extremely useful and Dr. Schuman will talk much more about this when we talk about progression of glaucoma, but this is really what we’re doing, we’re comparing that patient to themselves. Yes, they are different than average, we’re not sure if they have glaucoma, but if they change that may you now confirm the diagnosis once and for all, and that’s once again the value of getting good baseline testing, which is something that we do at UPMC Eye Center all the time, we get you know good baseline tests, and then we see if they change or not for that individual.

This, this graph is kind of a summary, this is actually relevant to the HRT but it brings back the OHTS Study, you know which the purpose of the OHTS Study was to determine if this population of high – people with high eye pressures, no visual field defects or definitive optic nerve abnormalities on baseline exam and the question was are these patients going to get glaucoma. A subset of this test, you know, of this study looked at patients who underwent HRT, about 25% of them. They went
in and they found that HRT was a very good predictor for whether these patients were going to develop glaucoma or not. An abnormal HRT made them much more likely to be likely to get glaucoma or to be diagnosed with glaucoma, whereas a normal HRT was more reassuring. And we’ve seen subsequent studies with that, with OCT as well.

So there’s been a number of studies, OCT versus optic disk photographs, which like it or not arguably are still the gold standard in assessing glaucoma. In the study by Zangwell 2000 there was a positive correlation between photographs and OCT, these other both functional tests, like FDT and SWAP, HRTGDX, OCT did a nice correlation with disease in a number of studies and once again compared to optic nerves another study shows similar findings. So that’s reassuring that once again come the gold standard, what we do looking at the optic nerve, OCT correlates well and this is with the, the older studies that looked at that. So when we look at other comparative studies to other imaging devices, OCT versus HRT we found good correlation with those as well. Once again these are, this is time domain OCT, the stratus you know that we are familiar with compared to HRT which are earlier kind of release technology. But the reassuring thing is that when you look at these devices there’s fairly good correlation in terms of being able to distinguish normal versus glaucomatous eyes.

So let’s talk more about what we are doing with, with time domain OCT, or the older technology. We get a signal, we need a scan around the optic nerves, and I bring this out basically to talk about the good and the bad things about with some of the older technology. You have to basically – the technician has to center the circle around the optic nerve, you need a good signal strength or you can
get unreliable data. And we’ve gone through a lot of this already. The diameter is 3.4 millimeters around the disc, it does ________ scans to give you information and then they give us a printout which we are somewhat familiar with.

Then what the device has to do is basically identify where it thinks the nerve fiber layer is. You can see that this graph is you know the nerve fiber layer should be thickest both at the superior and inferior poles, it will identify with these white lines and this, this scan, this picture from an older scan, and that will define the retinal nerve fiber layer.

And then it will give us a printout that we’re somewhat more familiar with, the TISNET plot, and it will basically scan the patient against the normative database and for glaucoma you know when you have the retina output to show the patients it’s actually pretty nice for CME, it’s pretty easy when you have your OCT of the macula you know you have a big hill here, it should be a valley, you have a big hill. Patients understand that, it makes it very easy to proceed with treatment. This is why we have to do things to you.

Glaucoma, sometimes it’s a little bit, it’s a little more obscure and subtle to find the differences, but I find these plots, and we’ve seen these with the newer technologies as well, useful for talking to the patients. And how I put it to the patient is like look, here’s a graph of you versus everybody else in the population. The green people are normal, yellow people are borderline and the red people are bad. And you are the black line. And you can see in these couple of areas you know in the middle humps there where you are kind of falling down in the red range, this is why, you know this is an
area where you don’t have as much nerve tissue as you should, and this is why we think you have
glaucoma or why we think we need to advance therapy. And when I put it that way clinically the
patients, it seems like they often will get it.

Then we have the output, which we are – the pie chart output which we are kind of familiar with,
looking at either clock hours, or the different quadrants, looking at average nerve fiber layer
thickness, once again compared to normative database. The nice thing about this output and
something that we always like to note is the mean, is the mean thickness. It’s kind of looking at mean
deviation on visual fields, it’s always a parameter we check, especially when we are comparing to a
baseline exam to see if that’s changed, because there is some other subtle things that may change on
exam but if the mean thickness is staying stable and the quadrants may be showing you know
transitions from red areas or yellow areas you don’t want to overstate the, the color coding in these
tests, and you really need to look at the raw numbers and put it in perspective. Because sometimes a
2 micron difference can flip a patient from one category to another in the normative database, and
you have to be a little bit careful with that.

And time domain OCT, you know which we are slowly moving away from, you know has a couple
in here. We’ll only talk about a couple problems with it. One is you know image quality, the poor
signal strength can give you abnormally thin values and you have to watch out for that in clinical
practice. And the other issue is really image registration or looking at changes over time, which can
be really pretty difficult with these devices in the long term.
So the signal strength, you want it to be at least over 6, and you want to be able – when you are comparing tests, you want to compare from one test to the next. And the important thing with that is that unlike other technologies which may just give you like a bad, fuzzy result, sometimes it can – it can process the information and give you an abnormal thinning. And we did this study back 5 or 6 years ago when I first got to Pittsburgh where we did it looking at corneal drying and the affect on signal strength. And you see that as your cornea gets drying the signal strength tends to weaken and you basically can see thinning of the output value or the measurement of the nerve fiber layer, you know. So this artifact is something you have to be aware of in clinical practice, and a good imager will know that you have to keep the cornea well lubricated. So what you don’t want to do is one time do the OCT right before the patient walks – as they walk in the door, and the next time do it after gonioscopy, pachymetry, you know applanation tonometry, it’s unlikely that the signal strength will be similar between those two exams. So it’s just something to think about in terms of image quality making the transition.

The other issue in the older technology, what some of the new machines have kind of solved in some ways is really the centration of the circle. With the old time domain OCT it’s kind of a manual process, and it’s technician dependent, and we see that – we saw and I still see a number of referrals for this from time to time, it changes in the measurement of the nerve fiber layer. So nerve fiber layer thickness is going to be thicker as you get closer to the optic nerve, so you really have to pay attention to the centration and how well that 3.4 millimeter circle, how close it is to the optic nerve or not. So as it moves away from the optic nerve, it – the nerve fiber layer will be thinner, and as you get closer it will be thicker. So if the centration is varying from visit to visit, which is certainly
possible, you’ll see variation in one quadrant. The useful kind of double-check against that is to watch what the mean thickness is doing. If the mean thickness is staying the same but you see the transition from, put it simply from green to red in its empiric quadrant watch what’s going on in the inferior quadrant. So that if it went from 80 microns thick down to 60 superiorly, but conversely the inferior got thicker, it went from 80 to 100, then you know that there is likely a centration problem and you largely don’t want to make a judgment based on that change that we’ll see. So once again, it’s kind of a problem with time domain OCT, which needs to be controlled for.

So the attractiveness and we have many vendors here today with their machines which you know I think is worthwhile to go and compare the plusses and minuses with these machines, with the newer spectral domain technologies. So the pluses with spectral domain for glaucoma tend to be less – a lot of it is just it has faster acquisition times, about 100-fold faster than time domain OCT, that inherently gives you less artifacts and also allows you to collect a lot more information. The amount of information that comes out of a scan with these newer machines is immensely more than what we got with the time domain OCTs.

The resolution of the structures is much higher, it gives us the information on different structures that number one, we never could look at before or really quantify. There’s interesting work, or increasing interest in measuring directly the retinal ganglion cell layer, which we know is what is lost anatomically in glaucoma patients. So it’s still in its infancy, but it’s been really interesting, we never could do that before. The software refinements are getting better and better and they have a lot of
different strategies for looking at that. The good thing is that some of the analysis is still the same, that we’re comfortable looking at when we are looking at outputs from these machines.

So when we look at reproducibly and the literature tends to support this in the study by Kim in 2009, they showed that basically just as we said here, reproducibility tends to be better. Once again, it’s really the speed of image acquisition for the most part. The nice thing in some of the technology, using the CIRRUS, for one of them you basically do a cube scan and then you can basically do postprocessing changes. You couldn’t ever do that before with the time domain technologies, and you can make corrections and adjustments for longitudinal comparison.

When you look at sensitivity, overall the study from Ho, you know what if you have a time domain OCT, now you are switching over to a spectral domain OCT, is the information going to be comparable? Can you basically just step off and move forward? The answer is probably not, there’s going to be some similarities and it’s reassuring when you compare them side by side, spectral domain tends to give thinner nerve fiber layer measurements than the time domain, so it’s not really a one to one correlation. It’s useful in a transition period probably to do both together at least once, but what we’ve found in clinical practice is after that one visit we basically use the spectral domain OCT machines and move forward with life. So you do lose a little bit of information when you do, when you transition over, but we think that the gains far outweigh that.

Some of the artifacts associated with eye movement in time domain OCT, one of the strategies to get away with that would be before the Spectralis you know uses eye tracking, the technology here, they
just do a single scanned circle as well, but with eye tracking it really does a pretty good job and gives you excellent image quality. You can get good images of the optic nerve and you can basically also get output of the retinal nerve fiber layer.

The interesting thing here is you can kind of see the Spectralis, their software, you know there is still a lot – you see a lot of the information, you see how squiggly the lines are. That comes from the blood vessels they are detecting. And in some ways it’s good because you are getting that resolution, on the other hand it’s somewhat disconcerting sometimes, we say why is it giving us such a squiggly line you know when the nerve fiber layer we assume and these, and one area to the next is relatively continuous. So it’s just different information from different machines.

The CIRRUS does a cube analysis so the same circle we see there can be placed post-processing, the changed information. So as long they get the image of the optic nerve in that picture we can, we can fiddle around with it later to get different information and post-signal acquisition. So it’s somewhat more forgiving if we didn’t get purple – perfect centration the first time around.

It also has this nerve fiber layer thickness plot on the top part, much as we’d seen originally with the GDX and that’s somewhat – sometimes nice to help us kind of quantify – or qualitatively give us an impression of nerve fiber layer thickness where the top colors are thicker, retinal nerve fiber layer, the cooler colors are regions with thinner nerve fiber layers and it’s nice to just glance back quickly, you see that nice bow tie pattern, you can kind of quickly make an assessment that everything seems to be there. And once again we have the familiar pie chart much as we saw with the old time domain
printout. CIRRUS has progression which Dr. Schuman will talk about a little bit more and we’ll talk about in our cases.

Another machine that’s available is with a different type of printout is the Optovue, and you see that some of the features are similar, once again the hot colors correlate with nerve fiber layer of thickness, also pie charts giving kind of average values across quadrants.

This is a bi – both eye printout. With the glaucoma we’ll see, and once again you’ll see that – you’ll see some differences in kind of mean nerve fiber layer thicknesses. Once again what you want to see is that the nerve fiber layer is thickest at the superior and inferior poles. You can see in this one there is some thinning there inferiorly and this patient with glaucoma that the values are thinner when we look down at the pie charts in, in both eyes. And this particular technology also has a change analysis where they’ve chosen in their printouts to put in differences from quadrant to quadrant, and kind of numerical values, so they will calculate the difference from visit to visit there.

So you know spectral domain OCT, there is somewhat limited correlation to the information that you had from your time domain OCT. Some of it correlates well but it’s not 100%, and a lot of times you are really reestablishing a new baseline in patients once you switch over to this technology. It’s also a young technology, it’s still evolving. We are gaining more and more information every day on this, you know where we are at UPMC Eye Center we are doing a number of studies evaluating this technology and it seems – certainly seems like it’s the technology of the future, but it is young. All the answers haven’t been answered in it today.
We worry about it hasn’t solved all the problems with media opacities or you know corneal scars, dry eyes, etc. That can still be a problem. There is certainly improvement in alignment and registration issues, the algorithms need to be further developed to continue to improve this, but the ones that we have right now are certainly promising and appear to have a certain amount of value, and for better or worse with this technology there’s a number of different manufacturers and they’ve all chosen different software, user interfaces to interact with the physicians and this is an opportunity but it’s also a lack of uniformity.

So in conclusion, OCT for glaucoma diagnosis it’s helpful, one again correlating to our functional testing, the visual field testing that is one of the standards that we still do on our glaucoma patients. It helps confirm our optic nerve changes, our findings that we have on exam. It can localize abnormalities, both in the nerve fiber layer and the optic nerve. And it basically helps us to basically make longitudinal judgments in terms of reproducibility of imaging, it seems that the sensitivity specificity may increase and newer software is certainly going a long way to make these newer, more powerful tools. And thank you very much.