The topic today is live donor liver transplant and I’d start this by saying that liver transplantation is really a victim of its own success. We’ve gotten so good at doing the procedure and the results are so good that so many people want a liver transplant. And if you look at what that means across the nation this is the number of people that are waiting and that’s increased and unfortunately the number of liver transplants being done in this country has not increased, it’s been relatively stable, and in fact in the last year the actual number of transplants done decreased. So what does that mean? It means a waiting list and what does a waiting list mean for an individual patient? Well the stark reality of the situation today is that at least in our region there’s about a 25% chance that if you are on the waiting list waiting for a transplant you will never get there, you will never make it to get a transplant, you will die from your liver disease before you get to the top of the list. So that’s the 25%, but what about for the other 75% who are actually lucky enough to get to the top of the list? Well even for them it’s not a rosy picture. It means a long waiting time before they get to a transplant and what that means is that by the time they actually get to the transplant, they’re in a very debilitated state, ravaged by the consequences of end stage liver disease and therefore they have a much more longer recovery and difficult recovery time after transplant.

This is data from our own center, if you look this is our median waiting time and what’s surprising is just in a period of about 2 years the median waiting time in the Pittsburgh area has almost more than doubled. This is the length of time that a patient sits on the waiting list before they get to a transplant. And this is our mean MELD scores and you can see that we’re now well above almost for the majority of our patients above 30 when we’re transplanting. And those of you who look after these patients know that there’s a big difference between someone who’s got a MELD score of 30
and someone who’s got a MELD score of 20, in the way they look, the way they behave, the way they act, etc., marked difference between them.

And unfortunately this is the national diagram of what MELD scores are like and there’s disparity across the region. UNOS is working to try to correct this but at the present time we are in one of the worst areas, Pennsylvania is this right here, and if you’re in dark blue that means that the mean MELD score is much higher, certainly above 30 when you’re getting a transplant. So that’s the caveat of all of this and recent changes in policy such as the Share 35, have only made this worse. It just means that we’re transplanting higher and higher MELD score patients. This is our wait list mortality in our own region and you can see it’s higher, higher than what the national average is. So we need ways to expand the number of transplants that we’re doing, the number of donors that we have. The biggest problem in transplant certainly in liver transplant today and in all transplants, is not rejection, it’s not infections, it’s, not enough organs for all the people that need it. And unfortunately we have limited number of ways to expand the number of transplants. Xenotransplant it’s still very much experimental, we don’t have a machine like dialysis that we offer for liver patients, marginal donors, we’re really at the limit, we already use them. And so really what we’re down to at the present time anyways, things like live donor transplants and split liver transplants and it’s live donor transplants that I want to talk about today.

So in my mind there are really a lot of advantages to a live donor transplant and I’ve just put them here on what the advantages are versus what the disadvantages are. And the advantage is obvious, if you’re in one of those 25% that’s never going to get to a transplant on that waiting list, if you have
someone who is willing to give you part of their liver and you have a life saving transplant, obvious advantages right there. But even beyond that there’s a lot of other advantages. It’s an elective, non-emergent operation. You can get that patient prepped and ready for surgery in the best possible way before getting to transplant. But much more importantly in my mind, a big advantage is the ability to transplant that patient at a lower MELD score before they get very sick. And as I said the difference between someone who is a MELD score of 15 and someone who is a MELD score of 30 is huge, and the ability for them to tolerate a major operation like a liver transplant is markedly different.

There’s minimal cold ischemia time so essentially you’re taking the liver out of one body and putting it in another so there’s minimal amount of time that that organ is deprived of blood and so there’s certainly advantages to that. There’s some immunologic advantages associated with it but not as much as with a kidney, but certainly there’s some immunologic advantage. And one advantage that’s not clearly realized by everyone is that for every one organ that you, or one patient that you transplant with a live donor, you actually free up a space on the deceased donor list for someone. So you’re taking patients off of the list and therefore, you’re decreasing the burden or the requirement for the deceased donor organs.

What are the disadvantages? Obviously the disadvantages are for the donor, this is a person who doesn’t need an operation, you’re not going to benefit them in any way, so you have to look at very carefully what are the short term and what are the long term risks to the donor because remember these are healthy individuals who are going to donate. You have to look at 10 years, 20 years, 30
years, what is there any impact associated with that donation process. For the recipient there are some other downsides to a live donor transplant. Remember you’re not giving them the whole liver, they’re only getting part of a liver, so there is, and even though the liver regenerates, there is at the initial time right after transplant, a period of decreased hepatic reserve. They don’t have as much liver reserve and some of that has implications as I’ll talk about a little bit later. And it’s technically a much more demanding procedure. You’re not having all of the blood vessel, you’re not having all of the bile that’s in there for there’s higher incidence of technical complications like vascular thrombosis and bile duct complications and it’s a much more technically demanding procedure with more at least a learning curve required than to some extent with a whole organ transplant.

So this is how live donor liver transplants started and it was where a generally a parent or an adult of some sort was donating to a pediatric patient and this type of situation we’re taking what’s called the left lateral segment that’s this portion right here. It’s roughly about 25-30% of the liver and you transplant that and this is what that operation looks like on the top two slides in the donor and then the bottom two slides the recipient. And this is a child who received a transplant from the mother and this is as I said this is the way that live donor liver transplants started. Kids were the most difficult to transplant initially with a deceased donor just because it was difficult to find a size matched organ to them, and it was most natural for a person to want to donate to a child. There’s almost always a parent available and obviously parents want to do everything and anything that they can to help their children. But just even beyond that and I’ll give you an example. Just recently you probably saw on the news we had a child that was in the foster care system, an appeal was made and
within a short period of time we had about 200 people that were inquiring about whether they could be a potential donor for this child, complete strangers who wanted to donate and help this child.

This is the national data that shows graph survival in living donors versus deceased donors and split donors in pediatric patients and you can see that especially in the very young children there’s significant advantages to a live donor transplant. Almost a 10-15% improvement in patient survival at early as well as carried on to late post transplant.

Now the problem or not the problem with this is that if you look at the waiting list at the present time, 90% of the patients that are on our waiting list are adult patients. Ninety percent of the patients that die while waiting for a transplant are adult patients. So if you really want to try to impact waiting list mortality you have to figure out a way that you’re going to help adult patients with this. Now if I was to take this very small portion of the liver, the left lateral segment and put it into most adult patients it generally is not going to be enough liver tissue enough for them until the liver has a chance to regenerate and they’re essentially in a state of liver failure because that liver is not big enough. So for most adult patients we have to use a bigger piece of the liver. The vast majority of the times we use the anatomic right lobe of the liver and that’s roughly about 60% of the liver that you’re resecting from someone and transplanting, but more and more we’re trying to see if we can use a smaller portion of the liver. I’ll talk about that, that’s the anatomic left lobe which is roughly about 40% and there’s some advantages obviously to the donor of doing that.
And if you look at nationwide, initially the vast majority of transplants that were done were for pediatric patients using a live donor, but in the late 90s we started doing this for adult patients and now in the U.S., I haven’t figured this out but, the vast majority of live donor transplants that are done are for adult patients. We have a very active program for both our pediatric as well as our adult patients and I’ll show you some data as to the numbers for that later. So the key part of this is donor and recipient selection, I’ll talk about each of those individually. Donor selection, there’s really several components to the donor selection process but essentially I divided it up into 3 process. The donor has to be medically fit, i.e., they have to have good heart, lung, etc., just like you would evaluate for any surgical patient. They’d have to be surgically fit and lastly they have to be psychologically fit.

So surgically fit to me essentially means that they have to have adequate anatomy and we assess this very carefully using various imaging techniques and this is very important that you get this ahead of time. You essentially want to plan that operation out before you get into the operating room and we use CT imaging and MR imaging to really give us a good roadmap. You need a good roadmap, you have to know what the portal anatomy is, the arterial anatomy, what the hepatic venous anatomy is, and what the biliary anatomy is. And this is just different imaging showing protal venous anatomy, hepatic arterial, hepatic venous anatomy, the biliary anatomy here and another key component of it is assessment of hepatic volume. So you have to have two components to this. The amount of liver that you give for the recipient has to be adequate volume for them, but just as important or if not more important the amount of liver that you leave behind for the donor has to be of adequate volume for them. And you can calculate this on imaging study, figure out exactly how much liver tissue that
you have and you can calculate based on the size of the donor and the recipient whether that's adequate for them. And so we essentially sit at a computer console and plan out our surgical operation beforehand and we go into the operating room and complete that operation.

One key component of this is that they have to be psychologically fit and this is very important, this is a key component of all live donor transplant evaluation that this has to be a voluntary procedure, they have to understand what the procedure involves, what the potential risks are and key to this they should not be coerced in any way. And I stress this though this is very difficult to do. So they may not be coerced in the financial sense but it's difficult to sort out whether they are being coerced just by the situation. And by that I mean if you are seeing a family member that's suffering and is close to death's door you know the situation itself is very coercive and it's hard to separate that out but we have a dedicated team with team members that understand and know how to evaluate this in a very good fashion.

Anyone can be a donor, generally it's family members that are donors for you but they don't have to be related to you. It can be friends, family members, church members and we often have unrelated donors and this is the data from the U.S. showing what the relationships are and you can see that while a significant portion are related there is a significant portion that are not related and I point out that case that I told you about earlier where we had a number of people that were complete strangers that wanted to be a donor for this child.
Just as important as donor selection recipient selection is also important. You want to choose the recipient's correctly and in broad strokes who should be considered? Well at least they have to be in some way meet criteria for a transplant, that they should be in your mind suitable for a deceased donor transplant. But more importantly is when should this transplant be offered? And I really set for myself an upper ceiling and a lower ceiling. So their circumstances have to be such that you would expect a meaningful recovery. This is not a procedure to do as a hale Mary type of situation, you have to expect that the recipient has a reasonable chance of making it through this. So even though you often see this situation where the recipient is at - really at very end stage the minimal chance that they are going to survive and the family members says well, doc, I don't care, even if there is a 5% chance that they can survive this and get through it I want to do it, you know It's my liver, I want you to accept me as a donor and you have to resist that temptation and say okay fine because a 5% chance of meaningful recovery is not meaningful recovery and it's not worthwhile in that situation to put the donor through the risk of a major operation.

So what's the lower and the upper? So there is an upper scale, the recipient has to have a meaningful chance of recovery. We generally set it at 30, we know that patients who are beyond a MELD score of 30 are at higher risk with this procedure because they need more hepatic tissue, more hepatic reserve and they are probably not as well served with a partial liver transplant. They have a much better chance of getting a deceased donor transplant but that's - some of that is just gestalt actually and it may not be true. If you look at the Asian data and in Asian countries there is no option of deceased donor transplant for these patients and they have to use a live donor even in those when
they have a lot of experience, even in these very sick patients you can get very good results. But generally we set an upper ceiling of 30.

The more important is the lower ceiling, when should we really meaningfully offer transplants to these patients? And Chris pointed out earlier that probably at MELD score once they are getting a MELD score of 12 or higher they are likely to get a benefit. But one thing I'd like to point out to you is that if you look at the majority of patients that die on a waiting list, and certainly this is the case in our own center, the majority of patients that are dying on a waiting list are not the ones that are very sick, the ones that have a MELD score of 40 and 35, the majority of patients that are dying are the low MELD score patients. These are patients with a MELD score between 10 and 20 that get some complication, a massive GI bleed, SBP, septic complication and they are just not able to recover because of their underlying disease. And so often I hear from either referring physicians or others that say well the patient is doing relatively well at the present time, I want to save that live donor option until later when they are really sicker, and that's the absolute worst thing to say to them because the best time to do a live donor transplant is actually when the patient is relatively healthier.

We know there is a survival benefit as soon as the patient crosses the MELD score of 12, so you may have patients that are let's say MELD score of 16 and 17, they look pretty good, they may be working still full time, they may be still doing all the things and say I don't feel too bad, and they have a option of a live donor available I think that's the time to consider it in those patients and let them know at least that this is an option, evaluate them. Because once they get a major complication then it's often too late to proceed with a transplant, and so often we see these patients, they had a live donor available, they get too sick and then the family member says to us well gees I wish someone
had told me about this later - earlier on because I would have been more than willing to give them part of my liver.

This was a recent analysis done nationally just to highlight this and I won't go through the details but the summary of this was that while with a deceased donor transplant it was at a cutoff of 15 that you saw a survival advantage with a transplant versus not. If you had a live donor and you had end stage liver disease decompensated, even if you had a MELD score of 10, if you had evidence of decompensated cirrhosis there was a survival advantage if you had a live donor transplant versus staying on a waiting list and waiting.

A little bit about the surgery of live donor liver transplant, as I said this is what the operation looks like. The majority of times it's the right lobe that we are taking and this is the portion of the liver that we remove. Essentially we remove it and provide inflow via the hepatic artery and the portal vein and outflow via the hepatic vein. As I said we plan the surgery ahead of time on a computer console and then go into the operating room and really just translate that and this is inside the operating room and the donor once we've split the liver into two pieces, the right lobe that we are going to remove and the left lobe that stays behind in that donor.

And this is what that operation looks like in the recipient side where we transplanted and connect it up to the corresponding structures. This is the right lobe and then as I said we are trying to use in situations use the left lobe and that's what the left lobe operation looks like on the right hand side of that slide. And this is inside the OR just to show some of the intricacies of it. This is the hepatic
artery. Connected to the hepatic artery much smaller connections than you would have with a whole organ transplant and right behind that is the portal vein and right anterior to that is the right hepatic duct that will drain the biliary system of that.

Okay, so let's talk a little bit about outcomes after live donor liver transplant. So remember when we talked about outcomes after this procedure we actually even though we started with one patient we have two patients at the end of the this. We have a donor and a recipient and you have to look at outcomes in both the donor and the recipient. And these are some of the things that we look at when we talk about outcomes in the donor. You want to obviously look at what is the complication rate, what's the mortality rate? But just as importantly you want to look at what are quality of life issues. How many of these donors are getting back to work? How long does it take to get them back to work? How many have long term impact associated with this because as I said these are healthy individuals that don't need an operation.

This is the worst possible outcome after live donor liver transplant. You may remember this case, this was in 2001. This was a brother who donated to a brother in New York. The recipient did well after the surgery, the donor unfortunately died because of a complication within one week after donation. And this had a profound impact on live donor liver transplant in the United States, live donor liver transplant was increasing rapidly up until that time. We were up to doing somewhere between 5 to 600 cases nationally per year and immediately after this event the number dropped to below 200 and since that time it's really stayed at that and we are doing roughly about 200 to 250 live donor liver transplants in this country. To put that into perspective there is centers in the Far
East in Korea, in India, centers alone that do well over 300 live donor liver transplants a year at one center alone.

This is the national data, so roughly about 4,000 liver donor liver transplants that have been done in the United States. There have been 5 donor deaths reported, 4 were early deaths directly related to the surgery giving roughly about a .1% incidence or risk of mortality and 1 late death which was a suicide 2 years post. Additionally there were 2 donors, there have been two donors where their liver remnant was not adequate and that failed immediately post-donation and they underwent a transplant themselves. Just to put that in perspective kidney transplantation is very well accepted in this country, there have been actually deaths after kidney donation between the year of 1999 to 2001 there were 3 deaths associated with kidney donation in this country.

Complications associated with this procedure, we generally tell donors that there is roughly about a 30% risk of a complication after this surgery though only about 5 to 10% major incidence of complication, and the most common major complication after this is a bile leak in the donor after this procedure, and you can imagine as you are splitting across the liver you have millions of tiny little bile ducts that you are dividing and there is potential for a leak from one of those.

The liver regenerates very quickly, this is some data that we have looking at liver regeneration in different patient groups but you can see that donors within a period of about 8 weeks generate to roughly about 90% of their original liver volume. And this is some data on recovery times and so that's very important to look at. Most patients are - most donors are in hospital for roughly about a
week after donation and are usually back to work somewhere around 2 to 3 months after the donation process. And then said it's important to look at what are the long term outcomes in donors 10, 20, 30 years and we're one of the main centers that are looking at quality of life evaluations in patients many years after the donation process.

Important to look at recipient outcome also. So this is national data. On the right is the most recent national data and you can see that there is roughly about a 10 to 15% survival advantage both in terms of patient and graft survival with a live donor versus a deceased donor transplant and our own data shows roughly the same thing. The green curve shows the outcomes with, with a live donor, the blue with a deceased donor and you can see that there is roughly about a 10, 15% difference in outcome. Now I would take this data with a grain of salt because essentially you are comparing two different populations here. The deceased donor patients are generally sicker, they have higher MELD scores when they are getting their transplants. The live donor patients are healthier, etc. when they are getting their transplant. But to me really that's not the way to look at it, you have to look at it as to what's available for the patient. Remember there is still the factor of a 25% waiting list mortality to factor in there, and the option for an individual patient when they come to see you is not a live donor versus a deceased donor right now, it's either a live donor right now if they have that option available or a deceased donor when they get sick enough to get to the top of the list. And the key thing, when they get sick enough to be at the top of the list and that could be 2 years down the road.
This is national data again looking at outcomes and this is just to point out that this is a technically demanding procedure, there is a higher incidence of complications especially bile leaks after this procedure. And again that's because you are dealing with partial structures as opposed to whole structures. And we tend to see newer problems that we don't see in whole organs including this thing called small-for-size syndrome which is essentially a condition where that partial liver is not meeting the metabolic needs and demands of that individual recipient and they have this prolonged recovery until that liver has a chance to grow and regenerate.

Important to look at the psychological outcomes of this and I just showed this case, this was a young girl who donated to her sister who had amyloidosis and this is the two of them on the wedding day which was 2 years after the transplant and I won't tell you who is the donor and who is the recipient, they both look pretty good and they are both doing very well.

The keys to success of this, A, it's a very as I said technically demanding procedure so really a good operative procedure is the sort of the anchor to this. You have to have a good enough graft volume, you have to have a good bile duct anastomosis, good outflow, good inflow; but just as important you have to have a great team and it's not just the surgeons that are part of this, it's the hepatologist, the nurse coordinators, the social workers, everyone is a key member of this and they all have to be unison in dealing with these patients to ensure a successful outcome.

If you look at the national data as I said the number of transplants, live donor transplants has gone down and it's really pretty much stagnant, somewhere between 2 to 300, but we are a national leader
in live donor liver transplants across the country because of this dedicated team approach that we have. We are the only center in Western Pennsylvania that offers live donor liver transplants, roughly about half of the live donor liver transplants done in the State of Pennsylvania are done here in Pittsburgh, 7% of the national volume for live donor liver transplant cases are done here.

If you look at the number of transplants done, roughly about 5% nationally, 5% of transplants are done from live donors, 95% are from a deceased donor. In our center last year 50% of the live - of the transplants that we did in pediatric patients were from a live donor, 25% of the transplants we did in adult patients were from a live donor. And that's just I think a reflection of the expertise of the dedicated team that we, that we have here.

So just to summarize a couple of key things. The advantages in my mind for live donor transplants that you can transplant patients that have low MELDs that are in relatively - but that have bad prognostic signs, you can transplant patients that have metabolic and rare diseases that don't fall in UNOS criteria. International patients, this is the best way to transplant them because you are not utilizing organs from a local source and there are several cases where you can offer this to options to patients that wouldn't actually qualify. And let me just give you one example.

So this was a young girl who came to us. On the imaging here this is a large HCC, the liver is entirely replaced by tumor. She would never qualify for a transplant by UNOS criteria. You know you have that Milan criteria, well she is way beyond Milan in all scenarios. The only option for her was a live donor transplant. We did what Dr. Hughes had mentioned to you where we sampled this
tumor and found it to be - have genetic markers that were favorable for that and her brother went on to give her a transplant and this is them just 3 months when I saw them in clinic last week. Both doing well, obviously long term results we'll see but for a young 30 year old girl with a tumor like this this was really the only potential option that she had.

We offer this option now even if you are ABO incompatible we can do a live donor liver transplant using this protocol and I won't go into detail of this but again this is just a way of trying to make and take down barriers of who is eligible for this procedure. We are trying to utilize smaller and smaller portions of the liver so that it's more easier for the donor utilizing this the left lobe instead of the right lobe, we are removing only 40% of the liver and this makes for a quicker recovery for the donor.

So I think just to end by saying A, there is a lot of advantages I think to live donor transplants. In many ways you can get better results mostly because you are able to offer this to patients when they need a transplant as opposed to when they need a transplant and they get to the top of a waiting list.