

LIVER RESECTION AND IMPLANTATION OF AN INFUSION PUMP  
Wake Forest University Baptist Medical Center  
Winston-Salem, NC  
Broadcast October 27, 2004

NARRATOR

After overcoming Colon Cancer David Michael thought that he was finished with the disease, until a cancerous spot appeared on his liver. Colon Cancer had spread. That is when physicians Wake Forest University Baptist Medical Center, determined that the best option was to remove the diseased section surgically.

PERRY SHIN, M.D.

Colon and rectal cancer is unique, and even though it has spread to another site, if you surgically remove that site, there is a significant number of patients who can benefit from that, and can survive long-term even after having had spread of their cancer.

NARRATOR

Liver Resection surgery is less risky today than in the past. With the increased knowledge of Liver segmental anatomy, combined with technological advances, the surgery may be a potential cure for many patients. During the next hour you will see surgeons at Wake Forest University Baptist Medical Center perform the procedure and implant infusion pump, to deliver chemo therapy directly to the affected area.

This live web cast from Wake Forest University Baptist Medical Center in Winston Salem, North Carolina, is part of the medical centers ongoing effort to bring the latest in medical care to patients, and medical education to health care community.

RUSSELL HAWERTON, M.D.

I would like to welcome you here to Wake Forest University Baptist Medical Center. Our colleague Dr. Perry Shin and Dr. Ed Lavan have been operating on this patient from earlier today, to perform liver resection for this colon cancer metastases. This is a common problem, colon cancer affects about a 150,000 patient per year and about half of those people will be at risk for recurrence, and of those 70% will be primarily in the liver. That leaves about 9 or 10,000 patients per year who may have liver metastases in the colon. This procedure started several hours earlier today and Dr. Shin has performed

initially an ultrasound of the patient, and perhaps we can go to that now so that we can see what this particular patient has in the liver.

It appears that we that we're not quite ready for that, so let me talk to you about what normally happens to people with colon cancer metastasis to the liver. Untreated they have a relatively poor survival of 5 to 10 months. We have very good Chemotherapy today and it's been proving over the past 5 to 7 years, however even with modern Chemotherapy, the average survival is only 15 to 20 months. With Chemo therapeutic treatment, 5 year survival is not good, just a few percentages of people will survive 5 years, however at the time of death 30 to 40% of people will have only liver disease which would suggest that those people might be cured by resection, and now we'll go to the tape of our ultrasound.

PERRY SHIN, M.D.

What I've done here is partially mobilized the liver, we still have some more dissection to go, but I'm using interoperate ultrasound to look at the hepatic veins and get more information about the anatomy of the liver as we proceed though our dissection. You can see right there, that large black structure on the ultrasound represents our left hepatic vein. This helps guide us in our dissection, as we go through some scar tissue this patient had a previous liver dissection about a year and a half ago. You can see an image of one of the liver metastasis in the upper right hand corner of the screen. It's usually denser than the background liver tissue.

RUSSELL HAWERTON, M.D.

I think you have before you now a slide, which shows the outcomes for a group of patients with colon cancer metastasis to the liver. I think you can see that in those patients whose liver lesions were not able to be resected, immediate survival is poor of about 7 months. If you look however, at the bottom of the graft those patients who were able to be resected with what we call negative margins or clean margins free of cancer, have immediate survival of 5 months for the first time have a survival rate of 5 years of 38%. So if Doctor Shin and Leven are successful today they offer this patient the chance at long term survival, something that no other therapeutic option can offer.

Colon cancer metastasis to the liver, present in several ways patients usually have a history of rectal or colon cancer. There is a cerium marker or CEA, which is followed often in patients who have had colon cancer, and a rise in this may suggest that there is a colon cancer metastasis. About a quarter of the patients who present with a colon cancer will present with a cancer liver metastasis at the time their cancer presents. We use CT scan as our primary modality of imaging to find these lesions and I believe you have before you a picture of a current CT scan, which gives us excellent imaging of the liver, and it allows us to plan surgical procedures such as that one today. We use other modalities such as PET scanning, or Positron Emissions Tamography, to look for the possibility that there is disease outside of the liver. The basic premises of surgery for

colon cancer metastasis to the liver, is that there is no disease other than in the liver, unless it is a synclines disease in which case the premises, the primary disease, is controllable as well. Several other factors are important when planning surgery on the liver for colon cancer metastasis. The patient has to be fit for surgery, and able to withstand it. One needs to be able to remove all disease from the liver and yet leave behind enough liver for the liver function to be adequate during the recovery and regrowth. As well, the tumor needs to be of the sort that one might expect favorable biology so that local resection might impact survival. We evaluate these people extensively prior to operation with a cardiopulmonary evaluation and extensive CT angiography within a short time frame prior to operation, to assess for technical anatomical factors related to resection, and also to assess for extra hepatic disease. We generally require that the patients have had their colon screened within one year to ensure that there is not disease in the colon at the same time. We generally do not need to biopsy a lesion, if it appears to be technically favorable. Investigators have come to know in great detail the surgical and vascular anatomy of the liver, and I believe you have before a slide that degenerates the inflow tracks in purple of the right and left portopaticalse and the outflow tracks of the hepatic veins in blue, and these allow us to plan our resection. The resection Doctors Shin and Laven today is of the left part of the liver, the segments 2, 3, and 4 as delineated there. I believe you have before you now a slide, which shows the anatomy of the bifurcation of the portopetacles and how we access then for vascular control. Earlier today Dr. Shin performed vascular control of the inflow to the liver and perhaps that is ready to show you know at this time.

PERRY SHIN, M.D.

What we have here is the left portal vein, we have the stapler across the left portal vein and what we're going to do now is go ahead and staple it off. We've closed it. Go ahead and press the button. Now go ahead engage the stapler. Close the stapler. Just fire the stapler. Fire the stapler. Keep going. Keep firing. Keep firing. Two of them together at the same time. O.K. so that's the left portal veins been stapled off. That cuts off the inflow blood flow to the left liver, and later on we'll see there will be some probably escemick changes to the left lobe of the liver. You can see here the staple line, that's the proximal, and there's the distal aspect. This allows us to transect the pretty large blood vessel in a pretty quick and safe manor.

RUSSELL HAWERTON, M.D.

That was the transaction of the portal vein to the left lobe of the liver of course, inflow to the left lobe of the liver includes also the hepatic artery, which was previously divided, and the bile duct which will be divided during transaction. We also divide the outflow of the lit segment to be removed, usually prior to transaction, we call that extra hepatic control of the veins, that would be the left hepatic vein transaction, we do that prior to perancial transaction which is actually dividing the substance of the liver. The slide you have before you now, which shows the substance of the liver to be divided, essentially straight down the middle between the main trunk at the bottom and the top. But before

we would do that we would divide the left hepatic vein and we also I believe the tape of that which Dr. Shin performed earlier today. That may be ready to go at the present moment.

PERRY SHIN, M.D.

We have the stapler across. So what we're going to do here is... come across the , so we've come across the vessel we're going to engage the stapler, It's fired now we just pull back. That shows that the left hepatic vein, middle hepatic vein trunk has been transected. Give some suction. Again, this makes the whole procedure a lot simpler, verses having to tie it over with vascular stitches. Right angle. Little bit left behind there. Metts, there's a little left piece left. Need a two O tie and a passer.

RUSSELL HAWERTON, M.D.

After completing the inflow division and the outflow division and having previously delineated exactly what segments of the liver to be removed we then moved to the poranckels section. That is the part that doctors Shin and Laven are working on now, and I'll ask them to let me know when they are ready for us to cut to a view of that. In the mean time I'll describe for you some of our further technical maneuvers in reseking the liver. Even with inflow and outflow division of the blood vessels, there is still cross circulation from the remaining right lobe of the liver, and we use a technique of low CVP, Central Venous Pressure, to reduce back bleeding, from cut hepatic veins during peanceal transaction. We place the patient in trendelenburg, or head down position as the sentralvenious pressure is often near negative and we want to prevent in training of air or air embolus when hepatic veins are open during the transection. We tolerate a low urine output to keep a low pressure in the sentralcirculation to minimize bleeding. Sometimes preoperative blood storage is used. In certain situations we use ore operative or intraoperative diagnostic laparoscopy to confirm the presence or absence of disease outside the liver depending on our suspicions prior to beginning. This particular patient had previous surgery and was not a candidate for such. If we do so, we examine the parentneal surfaces and the portahepatis and we perform an intraoperative ultrasound of the liver via the laparoscope's, to confirm the surgical plan. We generally make a sheveraon incision or an extended right sub costal incision and we mobilize attachments of the liver to the retroperitoneal on both the left and the right. These are the triangle ligaments. We also performed a maneuver called lowering the higher plate, which is ensiling the capsule of the liver at the base of segment 4 just above the bifurcation of the portopetacle. All of these maneuvers allow us better access to the liver to fully evaluate it and control o it's major vascular structures. As we described earlier we control either the left or right portal veins, we control the outflow tracks. I believe that you saw Dr. Shin use vascular staplers, which have improved our technical ability to do so at lower risk. The techniques of transection of the paramecium very, there are devices that provide energy to the liver to coagulate the surface to prevent bleeding even with inflow and outflow occlusion. Tissue linked provides one of these devices, as well as the technique of crushing the tissue with a Kelly Clamp, and then placing small clips across the

identified blood vessels is called crush clamp. We sometimes use occlusion of blood to the remaining liver, in this case that would be the right side. This would be called the Pringle maneuver, and it does commit the remaining liver to a period of warm ischemia, we try to keep this down to a minimum, but imbalance to prevent further bleeding this is often useful. I have before you now I think a slide that would show a typical resection specimen of the right lobe of the liver the white shaded area is the tumor and the raw surface is the cut transection plane after the specimen has been removed. As mentioned in the prolog to this the safety of removing parts of the liver has dramatically improved over the past 10 to 15 years, an increasing number of resections are being performed as you can see from this graph. Now this graph would suggest that major resections are removed decreasing, those are the sections of an entire lobe or more. Instead our technical ability to divide the liver under control is improved we do more minor or segmental resections. You can see that the need for transfusion has decreased significantly, and the complication rate certainly remain relatively stable, but the mortality has steadily decreased from 25% down to about 1 or 2% this is a large series of patients from the Memorial Sloan-Kettering in New York, and our results would mirror this. Hepatic resection depends upon the ability of the liver to regenerate. We often remove enough of the liver that its function is temporally compromised, however if it is able to maintain stability for a few weeks it will regenerate. In the slide before you, you can see two serial CT scans over time, 5 days after an operation, one month after an operation, showing hypertrophy of the residual left liver in this case. Dr. Shin are we at a time are we should cut to the surgical field? Another slide before you now with further enumerate this numerically this improvement and the safety of hepatic resection. You can see that the mortality of all resections is 2.8%. For a full lobe the mortality is 4%, but for a lesser lobectomy the mortality is .5%. The complication rate is not trivial at 20 to 30%, but these are surmountable in the context of a potential lethal disease, expectable. However, even with expert resection of the liver, unfortunately we do get recurrences in the liver of colorectal cancer. Somewhere between 30 to 50% of patients who have a successful resection will recur most often in the remaining liver. We presume this is from microscopic residual disease in most cases. What to do to reduce this risk is an object of intense study at the present moment, and people often receive further systemic chemotherapy, however there is no standard approach, and there is limited evidence of efficiency. An approach that has been used is the delivery of chemotherapy directly to the remnant liver in what we call edge of infection, or Hepatic Artery Infusion Pump Chemotherapy. Hepatic Artery Infusion Pump Chemotherapy, was used extensively several decades ago primarily in an attempt to treat surgically unresectable disease. The modern use of this technique is typically a different setting that is for advanced disease when all current known disease in the liver has been respected and when our primary worry is the risk of recurrence. You may have before you slide which shows the basic principle a pop is buried beneath the skin and a catheter led from it, to the gastroduodenal artery. Material infused here will entrain into the hepatic artery and fill the remaining liver, in the diagram that would be the left liver. The basis of undertaking chemotherapy in this way is the previous observation that hepatic metastases receive their blood flow primarily from the hepatic artery, where is the liver pancreas receives a great fraction of its blood flow from the portal vein. As such, if one can deliver chemotherapy directly into the hepatic artery, you can expose the liver disease to very high drug levels while at the same

time exposing the liver to less toxicity, as well as if you choose an agent with what we call first pass metabolism that is metabolized by the liver initially. The systemic toxicity will be very low. The response rate to chemo therapy here are considerably higher some 40 to 60%. This would compare to 20% for systemic chemo therapy. Our infusion pump is an outpatient process once installed. It carries less complication rate than the percutaneous catheter means of delivering chemo therapy, and it provides for continuous infusion. The drug we use is FUDR, fluorouracil it's in the 5 fluorouracil family. It's cleared to 95% clearance and delivered on first pass and there for delivery by hepatic artery infusion results in a 400 fold increase in concentration the liver has compared to systemic delivery, and a 100 difference for 5 fluorouracil would be only 100 fold. However hepatic artery infusion chemo therapy is not without it's own risks. These agents are toxic to the biliary structures and if they escape perfusion of only delivered they will be toxic to the duodenum and the pancreas. Generally these complications, most severe of which biliary strictures stenosis reversible, and are dose related. When we seek to do this we isolate the hepatic artery proximal and distal to the take off gastro duodenal artery, and we divide the gastro duodenal artery to place a catheter in this so that blood will then flow only into the hepatic artery in the remnant liver. This is a schematic showing how this is done to divide multiple small branches that would run to the pancreas or the duodenum. I believe we have a video of Dr. Shin placing this catheter earlier today perhaps we can run it at the present time. The slide in front of you shows a picture of the catheter in place.

PERRY SHIN, M.D.

What we've done is dissected out the common hepatic artery right here, and this is the gastro duodenal artery, which feeds the duodenum and the pancreas. We've transected the left hepatic artery. This is the stump of the left hepatic artery. Here, you're on dissection, and this is the right hepatic artery. Which is heading toward the right hepatic lobe. We've taken all the collaterals and blood vessels that feed off of this, because we don't want any of the chemotherapy from the pump to infuse into the duodenum or the stomach so, once we place the catheter in the gastroduodenal artery then the hope is that it will only infuse into the liver. What I've done, here is the catheter, I've cut it to size, this is the beveled edge, these are the hubs. We're going to take some 2 o silk pre ties in a right angle for me. We're going to lay these underneath the gastro duodenal artery like so, just lay these out, another one. These will be used to secure the artery, the hepatic artery catheter. Of course, the worse complication is if the hepatic artery catheter comes out. So we don't want that to happen. So we tie it in pretty securely. These are laved out like so. So once the artery is in the vessel, then you tie those down behind the hubs. The tip of this is... we want the tip of this to be right where the gastro duodenal artery intersects with the hepatic artery. So I'm going to place this vascular clamp right at that interface. Alright so, let's get our catheter ready. Dr. Rodriguez you're going to take the sharp 11 blade and you're going to make a transverse resection and come in and come up come in and go away from yourself, like this. Come in make a small nick in the artery. You want to make it close to this. Pull it, vein pick. You're going to take that and feed it in. So I'm using the vein pick I'm tenting open the artery. Keep feeding it in. hold it, don't let go you don't want it to slip out. Now it's held in place I'll tie the first one. You

can see the tip. Notice that the tip of the artery catheter is right where we want, it at that junction right there. Of the gastro duodenal artery and the hepatic artery, so you can see one of the bevels is right there. So I'm going to tie. That secures, that will be one knot to secure that so that it doesn't slip out. We're going to tie a second one as well. You can let go. Here's the second one. You want to tie that one? That should be right behind the bevel. Pick up to me. You're right in front of it now. So I'm going to push in. I'm going to come right behind that bevel. And catch part of the vessel. I'm going to catch part of the vessel. Tie it just right, don't over tie it. That looks good. Just three knots are good. Ok now that we've tied that, we can release the vascular clamp. Now we know that the tip of our hepatic catheter artery is right at that intersection. If your catheter is in too far and intrudes into the hepatic artery lumen you're going to get turbulence and you can get thrombosis of your hepatic artery. If the catheter is pulled too far back then you have some stasis in the gastro duodenal artery, and then you get thrombosis as well, so you really want it right at that junction. Scissors, ok now we're going to tie this down as well. So we secure it again and we're going to secure it one more time. Can I have a 3-0 silk either suture or either GI pop off either one. Again just right, don't over tie. This is going to be a fourth suture to hold this in place. Let me take a serosal muscle bite, on the duodenum. Cut this, why don't you go ahead and tie that as well. So it's a four suture we just have. Place great importance in securing the catheter and not having it to come out. Scissors to me. Ok, so that's the placement of the hepatic arterial catheter in the gastro duodenum artery, and that's the final position.

RUSSELL HAWERTON, M.D.

Now we're back in the operating room, and Dr. Shin is at a point in his transection where I believe that it would be best for us to turn the microphone over to him.

PERRY SHIN, M.D.

Alright we're in the middle of our liver transection we've come across most of the peracima on the anterior aspect, and now we're coming across some of the peracima more inferiorly. We're using the stapler right now. One of the larger vascular pedicles here. Probably about half way through the transection. We're using a combination of staplers, as well as crush clamp technique, as well as bimodal tissue monopolar cautery, as well as Kelly clamps. At this point superficially, this is our tissue, our monopolar it's a radio frequency device, it's got water cool tip so that we get deeper coagulation. Can I have the scissors? We're taking the right lobe of the liver. Excuse me, Sorry the left lobe of the liver. What this does is keep the tip cooled and we get deeper coagulation, when we come across the larger vessels. Kelly clamp. We would usually tie those or staple those. So really with the combination of techniques we can get through the liver in a finally controlled fashion. This right here that we're coming across the vessel, we've isolated it. Scissors. How's our frigate doing? With this technique here the object is to isolate the vessels and also bile ducts. This looks like it might be a bile duct here. We're going to clip this, and succors. And we're going to cut this. Why don't we have another stapler, a 60, 3.5 load it up for us, ok next. Looks like a small arterial bleed there. Could I get a 3-0 silk, stapler, 3-0 silk suture. We're about to go on pringul pretty soon. I'm going

to tie this bleeder off and then we'll go off. Scissors cut. We're going to hold some pressure here. And I'll let Dr. Hawertyon continued with the presentation. Once we get back on with pringel we will continue with the liver resection.

RUSSELL HAWERTON, M.D.

Patients that have isolated liver lesions and lung lesions removed, but I would emphasize that that is a rare situation. I think that Dr. Shin has reached a temporary holding point and I would like to talk to you more about how the hepatic artery infusion pump works. After that catheter is in place we need to confirm that it perfuses the liver, in its entirety, of the remnant liver and only the liver and we do that by injecting a fluorescein dye into the hepatic artery infusion pump and using a wood's lamp to watch the liver light up, unparticular, and also to ensure that the duodenum, stomach, and pancreas do not light up. This treatment strategy of hepatic artery infusion pump chemo therapy, in an ament setting, has been extensively studied at the Memorial Sloane- Kettering Cancer Center, in New York and they have undertaken a trial of patients who have had complete section of liver disease and then randomized them to receive systemic treatment and or systemic treatment plus hepatic artery infusion pump. And the most pertinent fact of the slide seen here is that the two year survival overall was improved in patients who received systemic chemo therapy and hepatic artery infusion pump chemo therapy 85% vs. 69%. Particularly significant was the improvement in absence of recurrent disease in the liver. 90% of the patients who had a hepatic artery infusion pump chemo therapy did not have recurrence in the liver, as compared to 57% of those who had systemic chemo therapy. The study was not designed to detect the statistically significant difference and overall survival, however a trend developed towards improved survival in those patient who had hepatic artery infusion chemo therapy and systemic chemo therapy. As you can see from the divergence of these two graphs here on the screen in front of you. To summarize our philosophy about surgical treatment of colorectal cancer metastases to the liver, if possible and in the appropriate setting surgical resection offers the best chance to these patients for a cure of this difficult disease process, and it can be performed with a relatively low morbidity and a very low mortality. However there is still a problem with tumor recurrence after resection and other treatment strategies are needed to improve this outcome. Hepatic artery infusion chemo therapy is one strategy that has an increased activity compared to systemic chemo therapy, and may improve survival. The combination of hepatic artery infusion chemo therapy and systemic chemo therapy might be expected to further improve survival. Here at Wake Forest University Baptists Medical Center and Comprehensive Cancer Center, we have several active protocols for patients with colorectal cancer with liver metastases. We have our NSABP, CI-66 trial of systemic cell platinum zaloda as well as hepatic artery infusion pump, FUDR after resection. We also have a ACOSOGZ05032 trial involving in systemic aranitecan and hepatic artery infusion pump FUDR after resection. I believe it's possible if you want to click on the screen, you can take a test on some of what's been described here. I would also be happy to answer further questions and we may see if Dr. Shin is at a point that would be appropriate for us to rejoin the operative field at his time.

PERRY SHIN, M.D.

This is the inflow to the liver and that allows us to get a little better homeostasis. As you can see, the liver is a very vascular organ. So we do everything we can to produce the blood flow during transection, now the pringle can't be inflow occlusion can't be sustained continuously, so what we do is intermittent occlusion, were we put it on ten minutes of occlusion and do our transection then five minutes off. And let the liver breath again, The liver can tolerate this, you can do this almost two hours if you do intermittent, if you do continuous inflow occlusion then you could only go about an hour or thirty to sixty minutes. I think with this last occlusion last pringle we should be able to get through the entire liver, get through our left lobe. Kelly clamp. Let us know when ten minutes are up. Kelly clamp. Got another 60, 3.5. This is a 60 mm stapler with 3.5 mm size staples. This is another lobe. Kelly crush clamp. Using the Kelly I'm just going to thin this out a little bit, staple. What we're doing is we're coming across. This one is not firing. Kelly crush clamp. Another lobe. Flip that. Scissors. The smaller vessels we can take.. The larger ones benefit more from the stapler. There is another small vessel. You have the stapler ready, Scissors? There's just some vein branches at the bottom. Another lobe. Almost through this we're coming to the back of this. With the stapler it is nice you can make a lot of head way. Staples vary in size as well, this one is for thick tissue. We have smaller staplers that are used for vessels. Neither one? We're really almost through this. Put a little pressure over here. Probably one or two more lobes and we're going to be threw this. One more lobe. We just got a little capsule left behind here. Stapler. This should be it. Could we get a small tag here? This is our specimen here, at least three metastasis lesions in this specimen right here. Let's hold a little pressure. We're just going to hold a little pressure right now. And then tackle the bleeders. We're going to come off pringle as well. Can I see the specimen please. Tonsils please. The tumor specimen is a... There is three of them here. What I'll do is ... do you have a 10 blade? I'm just going to open it I'm not going to cut into the margins so those are going to be ok for the pathologist. Just coming threw the liver right here. Pull over here Dr. Rodriguez . There's a couple of lesions that you can see. There is another lesion over here we can show you. Again, that's a good picture of one tumor there. Look's like we're about a centimeter away, right here. I delay you want to get a cm margin when your respecting these lesions. That's what we've got here. So this gentlemen, had synchronies liver metastasis when he had his initial colorectal cancer excision and it was excised, this is an actually recurrent tumor. Alright we're going to hold pressure here, got some sutures ready for us? Some 3-0 silk sutures. You can give back fluids if he needs. We've removed the left hepatic lobe and we've taken the pringle off so there is better blood supply to the right lobe and there is some bleeding at the edge but we've done using coagulation devices to stop the bleeding if there is any exposed vessels that are bleeding then we're over sewing those as well. Can I have a dry lap? So the bleeders are under control right now. We're just holding some pressure. What we do at the end is We also check the bile ducts are fully closed, and as a precautionary measure we will place a fibrin glue on the surface of the liver resection. Can I have a 3-0 silk suture? One of the best methods to control bleeding is to compress the liver tissue on itself. That's what I'm doing a with suture here. It's a blunt tip needle, but it's going to allow me to compress the liver tissue on itself. Cut. Liver tissue can be very pliable, so if you take to small of a bite

the sutures may just cut through. What this does is let me just compress using the liver tissue on itself an compress that tissue on top of that bleeding vessel. Looks like that took care of it. Most of the bleeding here is just oozing from the surface. Nothing really active right now. Now what we're going to do as Dr. Howerton has discussed in our presentation, even though we respected the tumors in the liver the rest of the liver there's a very high recurrence rate and the liver remnant has a high instance of recurrent disease. What we've done in this patient is a placed hepatic artery infusion pump and because of it's ability to deliver a high dose of chemo therapy directly to the liver think it may help to improve his disease free survival and maybe even overall survival. And we've already placed the catheter. You can see here. You can hold this back. And what we're going to do is test the perfusion with the Florien test.

RUSSELL HAYERTON, M.D.

Now I would mention to our audience that the space will be temporarily filled by the other abdominal organs. There will be no empty space there and over some four to five weeks, the remaining liver will regenerate to occupy a volume a proximally the same it did prior to resection. So it will fill the same space it did prior to resection.

Several other questions I've received from our audience, include how long does it take to recover from this surgery? The normal hospital stay would between 5 and 7 days. Most patients would be off of work for a total of six weeks before resuming their normality activity. After that they could be expected to be back to normal by that time their liver would have regenerated. There's certainly complications related to placement of the pump. If the pump perfuses anything other than the liver other words the duodenum, or the pancreas you can get severe pancreatitis or peptic ulcer disease. Even if it's perfusing the correct location you can get sclerosis or scarring of the bile ducts. This could lead to jaundice. If the pump were somehow to come loose, bleeding would be a problem. Occasionally there are mechanical complications related to kinks of the tubing and or infectious complications of the pump in the subcutaneous pocket. I think you see now the cut surface of the liver, were Dr. Shin has finished applying argonbeem coagulation. You can see the diagram in the upper aspect, as well as the beat of the heart against the diaphragm.

PERRY SHIN, M.D.

We're ready to test the pump perfusion as I mentioned before, it's very important the pump only perfuse the liver so we do this test were we inject floroceen die into the pump and watch for any extra hepatic perfusion if the duodendum or the stomach light up then we know that we've missed a collateral vessel. Really we should only see the liver light up with this test. Can you disconnect my head light please.? We use a woods lamp it's like a black light and, we'll go ahead and turn off the room lights. First we look at the base line, put he light over. Ok now we're going to inject the floroceen. You can see the

liver light up. You don't see much else. Mainly the liver so we're seeing mainly liver perfusion. The fluorescence is only in the liver. That tells us that there is no perfusion, the fat is yellow but that is its normal state with a black light. That's some staining from the surface. Alright very good. Lights on.. Patients get a nice orange urine afterwards. They really enjoy that. Do you have something to flush the catheter? I think with current treatment of hepatic colorectal liver metastases resection is the gold standard. The use of the hepatic artery infusion pump chemo therapy combined with systemic chemo therapy think represents one of the latest modality to treat people with this disease process. Hopefully it will improve the outcomes of liver resection alone. We do have a study open here right now using systemic irinotecan which is another type of chemo therapy given systemically with the intrahepatic FUDR, I think that represents a fairly promising approach to this very difficult and challenging problem.

RUSSELL HAWERTON, M.D.

Dr. Shin we have a couple of questions from the audience. Who are the candidates for this type of surgery? The candidates for this surgery are a subset of all those patients who've had colon cancer or rectal cancer whom have metastases discovered in their liver on follow up or initial diagnosis. The best types of doctors to diagnose this is would be whom ever is following a patient with colon cancer. Everyone whose had a colon cancer in general needs regular follow up to include screening of their colon with interval colonoscopy as well as imaging studies and blood studies. This could be a skilled gastroenterologist, medical oncologist, or surgeon. Whomever would be following a patient on a regular interval would diagnose a mass lesion in the liver, usually by an imaging study or CT scan. Those patients are often then referred to either a medical oncologist with expertise in colorectal cancer, and or a surgeon with an interest in liver disease, such as Dr. Shin, Dr. Levin and myself. I had answered it. Another question that comes from our office, if that the pump perfuses the right side of the liver, wouldn't the out flow of chemo therapy flow directly into the IVC and the rest of the body? Yes the out flow of the right side of the liver will flow into the rest of the body, but because of our choice of agent this particular agent is metastasize in the liver on the quote first pass, in other words the first time it goes through the liver. So that by the time you see blood leaving the chemo therapeutic agent has already been metabolized in the levels that the rest of the body exposed to would be relatively low. That's what makes the choice of agents so important in this setting. Another question is presented when the liver regenerates are the regenerated portions at risk to developing cancer? Certainly those portions that have regenerated like all of the liver remain at risk for further metastasis from the colorectal cancer. These would presumably be micro metastasis present at the time of resection which then grow after the liver is regenerated. 2 more questions, what is the life expectancy after this kind of surgery, and the life expectancy will depend upon the surgical margins to be determined on pathological review. If the margins are negative without evidence of tumor the patient may have somewhere between a 30 to 50% likelihood of long term survival IE five years. Of course the other 50 to 70% of the patients who develop recurrence and eventually be expected to succumb to their disease,

probably sooner than five years. Another question comes. Do they do this type of surgery of lung tumors? And I think that I addressed that previously, in a very select group of patients with colon cancer lung tumors alone will be the site of presentation maybe resected and an even smaller subset there maybe patients with tumors in the lung and the liver that are both resected, but this would be a highly unusual selected subset.

PERRY SHIN, M.D.

Do you have a couple of 2-0 silk sutures. I was going to go tissue length, but I need to go deeper. I'll give it something to hold on to. Clip the needle out, another one. Snatch both of them. This patient had another lesion in the right lobe, which we're removing. This is a smaller lesion, which requires a rode resection.

RUSSELL HAWERTON, M.D.

Another question is how long is the durability of the pump? The pump will usually function longer than the expected treatment strategy. It would be unusual for a treatment strategy using this pump to extend beyond six months. A subcutaneous portion if the pump can be removed at the conclusion of treatment. There have been patients who have had the pumps in that have functioned for considerably longer than this. Another question that comes from our audience is weather these techniques are used for primary liver cancer? The surgical techniques are all in use for primary liver cancer. Hepatic arthropathy infusion chemo therapy is less well developed in the setting of primary hepatocellular cancer for the primary reason that the drugs we have used with high first pass metabolism have typically been more active for colorectal cancer metastasis, however we have recently begun to use a protocol of hepatic artery infusion pump placement in those patients who have unresectable primary hepatocellular carcinoma in an attempt to convert them by response to infusion chemo therapy into a potentially respectable situation. The data for this is not as strong as for colorectal cancer metastasis at the present time. Dr. Shin is now removing a small lesion. That was present in what will be the residual right lobe of the liver. I order to render the patient disease free.

PERRY SHIN, M.D .

Let us know when ten minutes is up.

RUSSELL HAWERTON, M.D.

The question pertains as to what kind of lifestyle changes can the minimize the reoccurrence of liver cancer and with regards to colon or rectal cancer other than under taking a program of appropriate subsequent treatment, medical treatment follow up, there are no specific lifestyle recommendations to reduce the risk of follow up colon cancer metastasis to the liver, certainly one might reasonably avoid those agents majorius to the

liver, significant alcohol consumption. Those things that are behavior modifications to reduce the likelihood of colon cancer appropriate such as a high fiber diet. Another question, how do you refill the chemotherapy solution after the pump is implanted? There is an access port on the pump that can be accessed by a needle placed through the skin and in general these pumps are accessed every 28 to 30 days, depending on the time and appropriateness, the next fill of the pump is either with saline or an arête substance, or with chemo therapy. To begin a cycle of chemotherapy these are generally alternated. Dr. Shin is using a device called the tissue linknear which coagulates though transmission of energy through saline. Another question comes in, since the chemo therapy is going directly to the liver with small amounts going throughout the body, does this minimize the side effects of the chemo? And the answer is certainly yes. The purpose of this technique is to allow giving high doses of chemo theory to the let areas were occurrence would be expected such as the liver with minimal toxicity to other areas.

PERRY SHIN, M.D.

Do you have a stapler available? 2.5? Suction here.

RUSSELL HAWERTON, M.D.

Several other questions have come in, including are there patients who can not receive the pump, an if so what are the reasons? The pump does require an appropriate arterial conduits or gastro duodenal artery. There are anomalies in the blood supply to the liver, with either sensory or replaced right or left hepatic arteries and a certain select few of these may render the patient not a candidate for the pump, for anatomic reasons alone. Another question comes in, what is the pringel that is referred to in this surgery? It is a word for aclutting the hepatalduodenal ligament with a clamp this would include the hepatic artery portal blood flow that would be going to the remaining liver. This is after a famous surgeon named Pringel, and this was a described means of controlling bleeding in the setting of trauma to the liver. We use it in a planed fashion for liver surgery to create a more bloodless field during transection, however of course the liver is getting no oxygen at that time and this can not be continued indefinitely. We generally give it cycled fashion ten minutes on five minutes off, so the liver can breathe and drink during that five minute breathing phase. This prolongs our ability to use it repetitively. Dr. Shin is I believe using a stapler to transected the base of this new lesion.

PERRY SHIN, M.D.

I think that we discussed the benefit of hepatic resection some of the newer techniques that we've been using to facilitate liver resections and make them safer. Also discusses the use of the hepacrotill infusion pump, it is under investigation by national therapy board,

but I think it does represent a benefit in this selected location who are undergoing surgical resection, I know this therapy been studied in the past for unresectable disease and we don't know how it compares to some of the newer systemic agents but I certainly think in the averment setting when your undergoing resection or radio frequency ablation of liver metastasis from colon cancer, I think it is a viable option, I think it's very well tolerated. But it does require special training and very close surveillance.

RUSSELL HAWERTON, M.D.

We have one last question from the audience, what is the energy source of the pump and the rechargeable battery. No in fact the pump works on a hydrologic principal when it is filled the bellows are compressed under pressure and this is a calibrated expansion of this bellows fluid behind it at body temperature to slowly expel the material from the pump. I would like to thank all of you for coming to Wake Forest University Baptists Medical Center, via internet today, it's been our pleasure to share with you this area of our expertise and should you have any questions please feel free to contact Dr. Shin, Leven, or myself. Thank you again.