SHAUN MCKENZIE: Good afternoon. It's a pleasure to be here, and it's a great opportunity for me to talk about a topic that I'm actually passionate about, and that is patients with metastatic colorectal cancer. Today in particular, we're going to be talking about patients with synchronous hepatic metastases. This is that patient that gets their first colonoscopy. They find a biopsy proving cancer.

They're getting set up for surgery, they get that CAT scan, and low and behold, on that very first CAT scan they see masses in the liver. I think that traditionally, there's been a very nihilistic approach to these patients, but hopefully by the end of the talk today, I'll be able to convince you that we need to start looking at them a little bit differently.

So, the objectives today, we're going to review the literature that drives some of the controversies behind these approaches. Hopefully I'll put the role of surgery in appropriate context. I think it's important that we emphasize the multi-disciplinary approach, because the treatment of these patients can be quite complex. And we'll even just look at a basic scaffold of how, perhaps, in the future we might look at these patients a little bit differently and determine their best treatment strategy.

So I think the first question is, what is a surgeon doing talking about metastatic disease? Why would you ever offer surgery to a patient who has cancer outside of the place it started? And I think the key is biology. It's cancer biology that dictates how we address these cancers.

And what you have to understand is that, for hepatic metastases for colorectal cancer, the only potentially curative therapy is surgery. Before modern systemic chemotherapy was developed, five year survival after resection for these metastases was 25%. Five year survival for patients who did not have resection was 0%.

However, in the area of modern chemotherapy, survival for the exact same patient population has increased, and it actually continues to increase. It's been reported to be 35% to 58%. In all the recent series, survival is typically 50% or greater. Remember, these are patients that had a five year survival of 0% traditionally.

The survival is going up, as I said, but what's interesting is that the chemotherapy for this disease, while we refer to it as modern chemotherapy, it really hasn't changed much in the past 10 years. It's been about the same. A couple different treatment algorithms and treatment combinations of chemotherapy, and yet survival is going up. And one might ask, well, why is that the case.

And what has changed in the past 10 years is we as cancer surgeons have been starting to take a much more aggressive approach to this disease. And again, I want to reiterate that patients who are treated with chemotherapy alone are rarely, if ever, cured of metastatic colorectal cancer.

So, I think when you're listening to someone give a talk, it makes a lot more sense to understand their frame of reference. So, this slide here illustrates for you essentially the sandbox in which I play. These are the typical cancers that I and my partner will see in our practice. And if you go through and look at the survival, these are patients that were referred for surgery all the time. Patients with localized pancreatic cancer.

This isn't metastatic pancreatic cancer. This is CAT scan and endoscopic ultrasounds that show one resectable tumor in the pancreas. We do surgery on those patients and we can tell them that they have a five year survival of 18% to 25%, and their median survival is typically no better than 20 months.

How about stomach cancer? Again, typically treated with surgery. This isn't metastatic gastric cancer. This is localized gastric cancer. Five year survival 30% to 40%, median survival 30 months. Phalangeal carcinomas at the center of the liver, five year survival for resection, which is the only proven treatment for that disease, 25% to 30%. You're seeing the same numbers over and over again.

Esophageal cancer, five year survival after resection of localized disease. Again, not metastatic disease. This is localized esophagus cancer. Five year survival is only 30%. Hepatoma or liver cancer, we do a little bit better with a five year survival of 30% to 60%, but we know that most of our patients are cirrhotic and the recurrence rate is actually higher than 75%.

So, here at the bottom of the list of all these localized cancers that we operate on sits colorectal cancer hepatic metastases, stage four colon cancer, and we have a five year survival of 30% to 60%, and a median survival of 40 to 50, and actually, most recent studies is 60 months.

So again, why are we aggressive? We're aggressive because this is actually the one patient population that we potentially as surgical oncologists can help the most of all the patients that were referred for resection. Why are we getting more aggressive? It's not just because we like to operate, although we do like to operate. It's because the data is telling us we should be more aggressive.

This is a very recent study, but not so recent. I mean, it's a couple years old, but a series of 501 consecutive patients resected with colorectal cancer and they compared what were the standard sort of typical criteria for resection, which was one or two tumors, only in one lobe, one to two years after their initial cancer was identified.

They compared those patients to what they refer to as expanded indications, which would be metastases greater than 10 centimeters, bilateral disease, greater than four or five metastatic deposits. Some patients had over six tumors in their liver. 73 patients had disease outside their liver.

And what they found was that five and even 10 year survival was still excellent even in these patients that, again, had a five year survival of 0%, and of course 10 year survival obviously of 0% previously. The only independent predictors of survival in this series of 500 patients were greater than or equal to four tumors in the liver that were colon cancer or extrahepatic disease.

Notice that presenting with metastatic disease or synchronous colorectal cancer, which is what I'm talking about today, was not a predictor of survival. So, when we go to these tumor boards in these meetings, the number of metastatic deposits seems to be the focal point a lot of times. This patient has three tumors, this patient has five tumors, this patient has one tumor, and therefore we should operate or not operate solely on the basis of number.

So, this study has really tried very hard to tease out this question of number and how important the number of spots in the liver is. 484 patients-- And interesting here, this isn't even modern chemotherapy. So this is chemotherapy of 20 years ago, and five year survival in this patient cohort was 40%.

There was no difference in survival in patients that had less than four deposits and four to seven deposits. So now we're talking about not a cut off of four, but a cutoff of seven. But even in patients with eight or greater metastatic deposits, survival was 25%. Almost 50% of the patients in this trial had synchronous or colon cancer in the liver at the same time that their primary tumor was found, and it had no impact on survival.

So again, the data at surgical ontologists, as we review our data, it's telling us we don't need to be nihilistic. We need to be very aggressive in the treatment of these patients. So, let's get to know the patient population than I am in particular talking about today, and that is patients, again, as I described, who present, their colon cancer or their rectal cancer is found, and then they have imaging which proves it is already in the liver.

It's about 2,500 patients a year, and typically that's about 15% to 25% of new colorectal cancer cases. But if you look at the surgical literature, it comprises 25% to 50%. So again, at least in the surgical community, we are not bothered by the fact that these patients present with metastatic disease.

But as I started right from the beginning to explain, everyone has always sort of viewed these patients as a very poor patient population to treat with a very poor prognosis and aggressive biology. But is it really any worse than a patient who develops spots in their liver three years after their colon's been removed?

Of course there were many retrospective older studies that suggested that that was important, and they focused on this term called disease free interval, or the amount of time between their first colon surgery and their liver surgery, and they felt that that was an important factor. But again, once we got into the modern chemotherapy era, that became less and less of a factor.

And these or just a couple trials that are more recent. And all of them are basically telling you the same thing, and that is that there was no difference in survival and patients who have resectable disease when they present with their initial cancer or if that disease shows up years later.

And this is just one of the papers in the survival curve. This is one of the larger studies which compared 100 patients to 167 patients with synchronous or cancer at the time of their first diagnosis versus metachronous disease, or cancer their liver years or a year after their initial diagnosis. And you can see that the survival curves and the disease free survival curves are superimposable on each other.

So the naysayers will say, OK. That's all great, but this is a surgical paper, and therefore this is a highly biased report. Selection bias is critical to what we're describing. That led to this study right here. And this group looked at over 500 patients, and this time they specifically looked at patients who never had liver surgery. The only surgery these patients ever had was removal of their primary tumor.

And what you see is in those patients, whether or not they presented with metastatic disease, or they developed their metastatic disease later, the survival curves are superimposable. And note that no one who did not have liver surgery is alive at five years.

So, I think it is time to start thinking about these patients differently, and I think that most centers in the country are thinking about these patients differently. This table sort of has on the left side the classic sort of way we think about these patients, or maybe the way we did 15 years ago, and then the challenge to that.

And I think we won't go through every one of these in detail, but the patients who start out with unresectable liver disease. So, this is a patient that we see, we think there's no way we can remove all of their disease. Those patients used to always have their primary tumor removed.

There was this presumption that they were always going to become symptomatic from that primary tumor, and what we found is they actually rarely need to have their primary tumor removed unless it's symptomatic the day they show up and present. Patients with resectable disease, the way that we often will see these patients referred to us is, they'll be put on chemotherapy for years, and when their tumors finally start growing on chemotherapy, now they want to know if we can remove the tumor.

Well, the problem with that is, a couple years of chemotherapy is not well tolerated by the liver. So those patients often don't get offered surgery, not because they couldn't have, but now they shouldn't. And I think the other thing is this presumption that no one lives long if they present with metastatic disease. Hopefully I've already convinced you or at least got you thinking about the fact that that may not be true.

SPEAKER 2: How did the population that gets chemotherapy become less of a candidate? What is the-- the thing that happens in the liver is just not consistent wth your [INAUDIBLE] approach to this.

SHAUN MCKENZIE: So, the two treatment strategies that are most popular that have level one data to support them include two regiments. One is oxaliplatin and the other is irinotecan. Oxaliplatin causes sinusoidal injury within the liver, and those patients eventually will come to a point that their liver is so scarred and congested that it is unsafe to remove a significant portion of it.

Irinotecan causes steatohepatitis, and in those patients, they can behave very similar to a cirrhotic patient where, even despite the size of their liver, they don't have enough functional reserved to tolerate liver surgery. And so we will get to the cutoff point, but there is clearly a cut off point wherein any more chemotherapy becomes harmful and not helpful. It's a great question. Thank you.

So, this is a table that goes over patients that, in these studies, all have had unresectable hepatic metastases. And again, there's always been that presumption that these patients should have their primary tumors removed, and then if they can tolerate chemotherapy, that's great. But ultimately, nihilistic approach overall.

Well, if you look, you know this is obviously going down in chronological order. But what you notice is, as the chemotherapy regiments have become more aggressive, the amount of patients that required palliative surgery is going down. And in fact, in more recent series, the amount of patients that actually develop a symptomatic primary while on chemotherapy-- so it's not that they started symptomatic. They developed it-- is actually quite low. It's less than 10%, which, by the way, is in anyone's hands a conservative estimate of the morbidity of a colon resection.

So, you've got just as much a chance of having a complication from your colon surgery, if not more, than you would having your primary tumor become symptomatic. And so this led Memorial Sloan Kettering to specifically try to answer this question of, what do we do with the patients who clearly don't have resectable liver disease.

And they looked at 233 consecutive patients, and what they found was that in only 7% of patients was operative intervention necessary, again, as long as they weren't symptomatic from their primary at the time. And so what that tells us is, the best treatment for these patients who have systemic disease and are not resectable, completely resectable for potential cure, is to go immediately to systemically therapy and not to have a palliative colon resection first.

The other reason that's important is, unresectable doesn't always mean they're going to stay unresectable. The conversion rate of these patients to resectable disease in the liver and outside the liver in series is as high as 20% to 30%. So, there are still patients here that eventually may come to curative therapy who initially you never thought would be candidates for curative therapy.

And this study addresses that in particular, and this was a French group that was trying to determine, are we really curing these patients. Because of course, the nihilist in all of us, when we see patients with stage four disease, it knows that most of them will recur no matter what we do with them, or they will progress. They wanted to understand, how many patients are we really curing.

And so they started out with a study with a little over 200 patients, but ultimately they were able to cure-- and by cure, they defined as alive in 10 years or alive at five years with no disease at their follow up, and that happened in 16% of patients. So again, that sounds like a low number, but that's 16% of patients that were never ever going to be considered potentially curable in the standard sort of approach to this disease.

And this table over here on the left, I only put that in to show you, it is a job. I mean, if you're going to be aggressive, you can't throw the first best treatment at the patient and then when they recur say, well, that's it. We did our best. These patients oftentimes had multiple surgeries, had multiple rounds of treatment, and still were able to eventually be disease free at five years and alive at 10 years.

Some people have actually been so bold as to question whether or not chemotherapy is even necessary in these patients, whether or not surgery alone has cured it, and I think all of us that take care of cancer patients understand that just what you see on the scan in a patient with systemic disease, 95 times out of 100 is the tip of the iceberg and really do feel strongly that systemic therapy is necessary.

This is the study that actually definitively showed that the combination of surgery and systemic therapy is necessary. And again, it was 180 patients in each arm. All of them had to have a clearly resectable disease. They all had to have less than four or four or less metastatic deposits. And what they found was that in eligible and resected patients, there was a clear improvement in disease free survival. And this study sort of launched the thinking that you have to have both therapies to help these patients out.

What is interesting is in this trial, the trial design was chemotherapy before surgery and after surgery versus no chemotherapy. The trial was never designed to prove that you should give these patients chemotherapy before you operate on them, and yet that has been extrapolated from this trial, which is unfortunate because I think it really misses the main point, which is we're all in this together.

So the truth is, we probably don't know the best timing for when you give these patients surgery, when their disease is in their liver, and when you give them chemotherapy first. Surgery first or chemotherapy first. This was a study that, again, tried to answer that question, and what they found were that, in patients whose tumors grew while in chemotherapy, common sense, they did much worse and their five year survival was 8%.

After this trial, as you can imagine, neoadjuvant or chemotherapy prior to surgery become very, very popular. So, Memorial Sloan Kettering in response to that, because they're not proponents of chemotherapy first treatment for these patients, looked at their series, and they found that even in patients who progressed, if they stayed resectable-- here's the survival curves over there-- there was no difference.

And so chemotherapy really had no impact on telling you which patients were going to do well and which patients weren't. When you really look at these two trials-- and I think this is the challenge with trying to make sense of how we should manage these patients-- these two patient populations looked not much alike at all. The French trial had patients with greater than four metastatic deposits, a breadth of disease, extra paddock disease.

So these are patients that we would consider borderline resectable in the first place. This study out of Sloan Kettering, these patients had minimal metastatic disease. They were clearly resectable, and I think the point there is, they're not all the same. Every patient really needs an individualized approach, and we'll keep focusing on that as we move forward. But you can't compare apples to oranges and make a conclusion. And unfortunately in oncology literature, we compare apples to oranges quite frequently.

This is the slide that I hope further addresses the question that was asked previously, which is why is there a problem giving these patients too much chemotherapy? Why can't we just give them chemotherapy until things stabilize or start growing again, and then offer them surgery. And this is out of M.D. Anderson, their trial looking at patients who had less than eight cycles of chemotherapy versus patients that had nine or more cycles of chemotherapy.

And they found two important things. Number one-- and I'll start on the right instead of the left-- they found, as we described, the rates of hepatic insufficiency go up significantly in patients that have had greater than nine cycles of chemotherapy, which unfortunately, my partner will tell you, those are the patients we see most frequently right now.

However, complete clinical response or any beneficial clinical response-- So, this is you're giving them chemotherapy, you're getting serial CAT scans, and their tumors are getting smaller or maybe even disappearing. It didn't get any better after nine cycles. So, this sort of theory that more is better is wrong. Less is not always more, OK? And this is one example where that's the case.

So, you don't get any benefit in terms of treating the cancer, but what you do do is you cause the increased likelihood of complications. And anyone that has ever seen or been a part of the care of a patient that is having post operative hepatic insufficiency from a resection, it is a painful exercise for everyone involved, because the treatment for that is watching, and it is painful to watch.

So, what are the surgical strategies for these patients who come into the office with a colonoscopy and a CAT scan that show disease in both sites? There's basically three. There's the classical approach, simultaneous approach, and what's now become popularized as the reverse approach.

Classical is, get the primary out first and then come back later and treat the liver. The simultaneous approach is obviously, let's just get it all done in one surgery. I mean, why have two operations when you can do it in one? The reverse approach is focused on the fact that oftentimes these patients are not going to die from their primary tumor. They're going to die from progression in their liver. Therefore, let's get the riskiest disease out first and come back to the primary.

There's been a lot of data about simultaneous and stage resections lately. I mean, it's just exploded. I don't know when my group is going to stop writing about it. Hopefully soon, because I think the argument has sort of been won and lost about five times.

But the gist of subjecting a patient to a surgery that includes removing both a portion of their colon and a portion of their liver, in patients who are healthy, it's probably safe if both of those two operations can be done relatively safely. If either one of those two operations adds a level of complexity or is much more difficult, well obviously it's not going to go well if you try to squeeze them into one operation.

And this is probably the best study, even though it's a bit older. It's still probably the best one out there, and they divided patients into whether or not they needed a major hepatectomy-- so that's removal of approximately half of your liver or more in simpler terms, versus a minor hepatectomy, which is a small fraction of your liver removed with the tumor.

And they found that when you combine the major hepatectomy with the colon resection that your likelihood of mortality after the surgery or major morbidity went way up. And so what most of us feel is that if you have to do a major liver resection at the time of a colon resection, you really need to think twice about doing that. That's sort of the take home point for the surgical oncologists of the world.

But this has been argued about and refuted, and this is what you'll get in the literature now. You'll get a single institution series. This is out of University of Louisville, where they showed that didn't matter if we did a major hepatectomy or a minor hepatectomy, the outcomes were the same.

Well, the problem is, they wouldn't share with anybody what their selection criteria were for who they did what to, but it was clear that there were selection criteria. And I think again it gets to your ability to assess the patient and determine what kind of physiologic insult are they going to tolerate. But I think you have to proceed cautiously with certainty.

What is important to know-- and this comes out of M.D. Anderson-- is that terms of the potential for cure or for disease control, the surgical strategy does not make a difference. Whether or not you take the liver disease out first, you do all of the operations at the same time, or you take the colon out first, as long as you select the patients appropriately and don't lose them in the post operative period, the overall survival of any of those three cohorts is going to be the same.

And I think again, as everyone is pushed towards, we need to control the liver disease, we need to control the liver disease, the primary has all of a sudden become sort of an after thought. Well, that's where this all started in the first place. It's a colon cancer that spread to the liver, not a liver cancer that spread to the colon. And it is important to look at that primary tumor.

And this is a study that just showed how important what's happening at the primary tumor dictates how the patient's going to do. This graph on this side is patients who you can see one liver nodule, two to three, greater than four. All of these patients had less than three or three or less lymph nodes positive at their primary.

Now, you don't have to be a statistician to see that those survival curves are looking a lot worse than those. These are patients with four more lymph nodes positive. So again, we can't forget that, when you address this disease you can't just look at the things you can see on a CT scan. You have to address the whole disease or the whole patient.

So, I've talked about three surgical strategies as if that wasn't confusing enough. I already told you, we've got to get some chemotherapy in there. So, this is how mind boggling the approach to these patients can be. I mean, this was a mathematical model paper that was trying to look at the best approach, and they came up with 13 different potential strategies for how to manage these patients.

And this paper's kind of like getting a root canal when you read it, but I think what it does illustrate is that this is a very complex patient population and how you're going to help them the best is referring them to a group or to multiple cancer physicians who can work together to come up with a treatment plan instead of that sort of first tag it approach, which, I saw them first. I'm a surgeon. I'm going to operate on them first. Or I saw them first. I'm a chemotherapy doctor, I'm going to give them chemo first. I think that a multi-disciplinary approach is the way to go, and this is why.

It only gets more complicated. I think this is another patient population that you never ever would have thought we'd be talking about operating on. And this is an illustration who comes into your office, they have a colon cancer, and they have metastatic disease all over the place. However, as I told you, that may or may not be a reason to not potentially offer these patients curative therapy, and there are multiple strategies in order to clear these patients of disease.

And something that's now popularized is what's called a two stage approach where you take part of the disease out of their liver when you take their primary tumor out, then you embolize a portion of their liver so that that part grows, and then you go back in and take the rest of their cancer out at a later operation.

And so again, we continue to get more complex because we really feel that this is a patient population that we can help. So let's maybe illustrate certain complexities of this by going over a couple simple patients. These are all based on actual patients that have been seen in the region. This is kind of the ideal case we all wish we would see in our office.

It's a 51-year-old patient. His only medical problem is the anemia that led him to his colonoscopy in the first place, and he has a sigmoid colon cancer. And he gets a CT scan, and it shows a solitary spot in his liver. So, synchronous disease, solitary metastases. He's seen by all of us. We talk about his case in a multi-disciplinary conference.

And this is what you see. You can just kind of see that's smudge there. This is his primary tumor. You see a little bit of thickening and some lymph nodes, and then over here you see just one tumor on the back part of the right lobe of his liver. And so this is a patient that we felt clearly resectable disease, healthy patient. We can remove his liver disease with a minor hepatectomy.

Let's get all this disease resected and then he can get his chemotherapy without interruption. And so he underwent removal of the posterior portion of the right lobe of his liver. At the same time, he had a sigmoid resection. He did have a postoperative ileus, but otherwise did quite well, and he's currently just finished his six months of chemotherapy and is disease free at the moment.

So, that's a nice case. They definitely don't all come like that for sure. This is probably more commonly what we see. This is an asymptomatic primary tumor. So, this patient was just getting screening. He's 50 years old. This was his screening colonoscopy that he got for his 50-year-old birthday. Again, a little bit of anemia, but really that was sort of a finding after his colonoscopy, and he has a biopsy proven tumor seen in his ascending colon.

He gets a CAT scan and he has seven metastatic deposits in two separate spots in his liver, and this case was not here in Austin. This is actually case from the outside. But basically, when you look at his liver disease, he needed his right lobe removed, but then he had disease over here and he needed the lateral part of his left lobe removed.

And then of course he had a primary tumor that needed to be removed, so again, five, 10 years ago, this patient would've walked into someone's office and they might have been offered a fishing rod, or maybe they'd get systemic chemotherapy. But they took an aggressive approach in this patient, and so he got chemotherapy first.

Then he went to surgery and had his primary tumor removed and had the left section of his liver removed. Patient was put back on chemotherapy and has the portal vein to the right lobe embolized, which allows what's left of his left lobe, which is this section and this section, to grow so that we do have less likelihood of having liver failure post operatively.

Goes back and has his whole right lobe removed, and then this is only one segment of the liver. This is actually two. This is segment four, and this is what's referred to as a fuddy load, and this patient is alive and well just on those two segments. This publication, the patient was four years disease free at the time of this publication. So, again a patient previously never would have been offered treatment and is now at four years without disease.

This is another scenario. This is a 55-year-old, previously healthy patient. Very healthy, but all of a sudden was having fairly significant fatigue and just feeling exertion. And so finally he goes into his primary care physician's office who checks some labs and immediately sends him into the emergency room because his hemoglobin is six.

And then you start talking to the patient and you get that, oh by the way, I've been having liquid stools for months. He's admitted to hospital. He gets transfused, he gets scoped, he gets scanned. And what we found was one tumor in his liver. So we're thinking, hey. OK. One tumor in the liver. This sounds like one of those guys we could do in one surgery. It's pretty small.

But look at this primary tumor. This thing was as big as a house. It involved his bladder, his ureter, his small bowel. He had perforated it. And so what did we do for this patient? We didn't do everything in one operation, because this patient presented in an urgent or emergent fashion. Even though I was asked to do all of his surgery at once, I said, no. That's not safe.

We did a lap assisted resection of the sigmoid. We had to take out small bowel, bladder wall, part of his ureter. We put him back together. He had two metastatic deposits seen under laparoscopy in his liver. One of them you couldn't see on the scans. He recovered from that surgery actually quite well. He got four cycles of chemotherapy. We re-staged him.

He actually had a good response to treatment, and he's just recently undergone a laparoscopic left lobe resection of his liver. He's doing quite well, and he's going to complete his chemotherapy. So again, different presentation. Now, this is a patient whose primary tumor was making him sick. These are not the patients that we get so focused on the liver disease and forget the primary.

And then this is the last example I'll give you. This is in a whole other added level of complexity, because this patient had rectal cancer. So this was another healthy male who had rectal and anal pain and rectal bleeding, but he had no anemia, he had no obstruction. He gets a CT scan and he has multiple metastatic deposits, but most of them are in the right lobe.

He only had one in the medial part of his left lobe. His colonoscopy and his exam verified that he had a very low tumor and likely would need in APR or would need his bottom resected in order to get his disease out safely with a negative margin. And so these are just some representative scans, and what you see is, he had one tumor that was in just the edge of his left lobe. Actually, it's right here. I apologize.

And then he had multiple tumors in his right lobe. And you can just barely make out his cancer right down at his bottom there, and you can see some of his metastatic disease. So I had mentioned very briefly the reverse strategy, and this is a patient that we had planned the reverse strategy on. So, with that extended disease, you really need stronger chemotherapy than just the stuff they give with radiation.

And so he got four six cycles of chemotherapy. He was going to get a planned resection of his liver disease first, then go back and get chemo radiation, which is the standard of care for rectal cancer, and lastly, at the end of his treatment course, had his rectal cancer removed. So that's a patient that would be a good candidate potentially for the reverse strategy.

So again, I think if anything I've probably done is confuse most of us in the room. But this, again, sends home the point that these patients are complex, but there's a chance to cure them, or at a minimum a chance to help them live a long and happy life, but it is complicated, and therefore it requires a multi-disciplinary approach.

But this is just if you wanted to see behind the curtain what's going on in my head when one of them walks in the office. This was kind of what it looks like, unfortunately, for me. But basically, you start with synchronous disease and then you split off. Are they resectable, or are they unresectable in their liver? And based on that, you go down one branch.

But you always have that possibility that you may come back up and be reevaluated. You don't give up on the patient unless the patient doesn't want the treatment or it's clear that the treatment is futile. And sometimes it takes a while to really sort that out. But you can wind up with multiple different strategies but in the end, always a combination of surgery, chemotherapy, and if necessary, radiation therapy.

So, to conclude, colorectal hepatic metastases, while a clinical challenge, I hopefully have shown is a potentially curable surgical disease. Synchronous presentation-- again, that's the patients we're talking about today-- should not preclude an aggressive approach. In fact, if anything, we ought to maybe be more aggressive in those patients.

Patients with unresectable disease infrequently need to have their primary removed right off the bat. Usually, they should go right to chemotherapy unless they're symptomatic, and they may potentially be converted to resection candidates. And then most important is that the management of these patients is complex and really requires an upfront multi-disciplinary evaluation by both surgical and medical oncologists, and oftentimes radiation oncology as well. Thank you and I'll take any questions.

[APPLAUSE]

SPEAKER 3: Operating in the radiated field of the rectal carcinoma patient, was that a challenging event, or has it gotten easier now?

SHAUN MCKENZIE: I think it's easier because radiation therapy has improved so much, and we've become better at learning what time interval we should wait before we go back into the radiated pelvis. But I think the combination of improved radiation therapy and just a little bit more surgical experience has made it very feasible and doable. And in fact for most patients, that's how we would proceed with neoadjuvant radiation.

SPEAKER 4: Did you [INAUDIBLE] I assume they don't use it collaterally anymore or anything like that?

SHAUN MCKENZIE: In terms of resecting them?

SPEAKER 4: [INAUDIBLE].

SHAUN MCKENZIE: Well, so what those cases illustrated was, in patients where you know that you're going to leave a small portion of the liver, what you can do is remove the disease that's on one side and small, and then embolize the portal vein to the side of the disease where it's significant and you're going to take a large portion of liver out. That's referred to as portal vein embolization.

And in those patients, that left side, for example, will actually grow before the surgery so that when you remove that big piece of the liver, the chances of having liver failure are less. So that treatment actually doesn't treat the tumor. It just decreases the patient's--

One thing I didn't even get into here is the role of ablation, which maybe is what you're referring to, where we, instead of removing the tumor, will actually place a probe within that tumor and destroy it with either microwave or radio frequency energy. And that adds a whole other level of complexity to this, but it's certainly a weapon that we can use and perfect for the smaller tumors you're referring to.

SPEAKER 5: John, will you speak about that a little bit? You've been doing this long enough-- I certainly have-- that we should've seen the pendulum swing back in the '90s. The goal is preserving the paddock function. The road before the portal vein embolization is to try to shoot piecemeal at these and really, although that's huge, the emphasis has gone away from that.

SHAUN MCKENZIE: Right. I think that there's been-- I think when radio frequency ablation and microwave ablation became developed and popularized, there was a lot of excitement, because obviously if you can do less surgery and get the same results, why wouldn't you do that in a patient?

And the concept of just treating the tumor and not having to remove significant portions the liver was attractive. Well, that was developed for actually patients with hepatomas or liver cancer because they have cirrhosis and you cannot remove large portions of their liver. But it very quickly got extrapolated to metastatic disease here, and I think initially the data was promising.

And that's because it was short term followup. But what we've learned is that these surgeries that we do, even their outcomes are dictated by biology. And what I mean by that is, ablation strategies are more effective in hepatoma than they are in metastatic disease, and that's just the way the tumors behave.

And so the emphasis for using ablation strategies in colorectal cancer for liver metastases has gone away, and the main reason is that we're seeing that the recurrence rates in the liver are significantly worse than they are for patients with hepatomas and cirrhosis. And also, these patients should and most often do have normal livers, and that provides us an opportunity to be more aggressive.

And so I think again, as surgeons and as surgical oncologists like Dr. Flem and myself, it's our responsibility to not do the easiest treatment sometimes, but the best treatment. And I think radio frequency and microwave ablation have a very important role in this disease, but it's not the treatment of choice for every patient, and that's the important thing to remember.