Thank you, thank you and welcome everyone to Cancer Center, grand rounds and really pleased with how we continue to innovate on formats in this new Zoom World of the pandemic. And I think today’s session is going to be interesting given the nature of four speakers and various levels of their training and professional development and are. The great work that’s going on in...
radiology and biomedical imaging
and the science associated with it,
most notably in Interventional Oncology.
Please introduce let us say the
Doctor David Madoff is,
As you may recall from last week,
Doctor Madoff is the Co director
of Interventional Oncology of the
Interventional and college research
and the section chief for
Interventional radiology.
An Department of radiology
and biomedical imaging,
and David really has throughout his career have been an innovator in this space. And with his joining the faculty at Yale now a couple of years ago, I guess has really built out not only the capabilities in our clinical operations, but expanding research which is really exciting. And so David I turn it over to you to sort of introduce the other speakers and share with us all this great work. OK, thanks Charlie. So I’d like to again, thank you for giving me the opportunity to speak in Yelp, Cancer Center grand rounds. As you saw it last week I was part
NOTE Confidence: 0.8278826

00:01:53.741 --> 00:01:55.643 of a session on the multidisciplinary
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00:01:55.643 --> 00:01:57.689 management of colorectal liver metastases.
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00:01:57.690 --> 00:01:59.510 Today’s session, as you stated it will
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00:01:59.510 --> 00:02:01.549 be focused on Interventional oncology.
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00:02:01.550 --> 00:02:04.262 What it is in some of the exciting
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00:02:04.262 --> 00:02:06.678 research being done in our lab at Yale.
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00:02:06.680 --> 00:02:08.654 Therefore, this program will focus on
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00:02:08.654 --> 00:02:10.955 work being done by our trainees and
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00:02:10.955 --> 00:02:13.097 not really on my own personal work.
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00:02:13.100 --> 00:02:15.459 I will just be introducing the topics.
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00:02:15.460 --> 00:02:18.316 And our vision and goals for the
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00:02:18.316 --> 00:02:20.119 Interventional Oncology Program at Yale.
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00:02:20.120 --> 00:02:22.829 So this session, as you may recall,
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00:02:22.830 --> 00:02:25.014 was originally planned for March 10th
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00:02:25.014 --> 00:02:28.258 and it was just after the kovid pandemic.
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So interesting, Lee, It’s actually given us more time to make our data even more mature. So for the audience for today. So I’m really pleased. I think about that. So I’m going to start and then will be followed by Julia Shapiro, who happens to be the Co director of the intervention college. Live with me. He’s actually an assistant professor of radiology and biomedical imaging, while actually, and I are resident so that shows you the level of achievement that some
00:03:01.836 --> 00:03:04.374 of our colleagues really have and
00:03:04.374 --> 00:03:06.834 then will be followed by Jessica
00:03:06.834 --> 00:03:09.398 Santana and tells Evie who are both
00:03:09.398 --> 00:03:11.559 graduate students in our lab and
00:03:11.559 --> 00:03:13.869 the work will all be talking about
00:03:13.869 --> 00:03:16.129 liver cancer and Interventional
00:03:16.129 --> 00:03:17.986 oncology related activities.
00:03:17.990 --> 00:03:20.874 So let me just share my screen.
00:03:27.170 --> 00:03:30.610 OK, so. Really,
00:03:30.610 --> 00:03:32.250 what is Interventional oncology?
00:03:32.250 --> 00:03:34.395 Well intermixed oncology is a
00:03:34.395 --> 00:03:35.682 subspecialty of Interventional
00:03:35.682 --> 00:03:37.419 radiology that utilizes minimally
00:03:37.419 --> 00:03:39.063 invasive image guided procedures
00:03:39.063 --> 00:03:41.491 to both diagnose and treat patients
with various forms of cancer.

The benefits of primary intervention oncology treatments or its immediate tumoricidal effects.

As you I’m sure are aware, there minimally invasive, resulting in cost reductions and time Efficacy, as well as having minimal systemic side effects leading to an overall improved.

The goal has been to make the case for us becoming the 4th pillar of cancer care and over the years I believe we have and this has been shown actually in many ways.
These include having IO therapies incorporated into multiple NCCN guidelines which include colorectal metastases include HP be an even in renal cancer, having trials to assess the role of Percat Aneus management of cancer, and what I believe is most important. Is that, I believe now become a valued participator in most if not all of tumor boards. So what does it take to become a pillar of oncology? Clearly each clinical discipline needs to have a strong foundation in basic,
00:04:47.740 --> 00:04:49.184 translational and clinical research.
NOTE Confidence: 0.9124253
00:04:49.184 --> 00:04:52.499 We do have some work to do in this regard,
NOTE Confidence: 0.9124253
00:04:52.500 --> 00:04:54.845 but I must say I was really
NOTE Confidence: 0.9124253
00:04:54.845 --> 00:04:57.603 thrilled to see when I was in 2016
NOTE Confidence: 0.9124253
00:04:57.603 --> 00:04:59.979 as an invited faculty of Asco GI.
NOTE Confidence: 0.9124253
00:04:59.980 --> 00:05:02.220 My discipline next to my name was listed
NOTE Confidence: 0.9124253
00:05:02.220 --> 00:05:04.400 actually as an Interventional Oncologist,
NOTE Confidence: 0.9124253
00:05:04.400 --> 00:05:05.772 not an interventional radiologist,
NOTE Confidence: 0.9124253
00:05:05.772 --> 00:05:08.479 so I was really happy at that time,
NOTE Confidence: 0.9124253
00:05:08.480 --> 00:05:11.756 and I thought we actually made it.
NOTE Confidence: 0.9124253
00:05:11.760 --> 00:05:12.048 However,
NOTE Confidence: 0.9124253
00:05:12.048 --> 00:05:14.640 I really do believe that in terms of research
NOTE Confidence: 0.9124253
00:05:14.699 --> 00:05:16.729 and education of referring physicians,
NOTE Confidence: 0.9124253
00:05:16.730 --> 00:05:18.385 I think we’re nearly there
NOTE Confidence: 0.9124253
00:05:18.385 --> 00:05:20.040 and on the right track,
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00:05:20.040 --> 00:05:24.369 but I don’t know if we’ve come there totally.

9
So here you can see a long list of procedures that we do, and I owe. These can range from image guided biopsy, primary tumor therapy, palliative procedures, central venous access, managing of complications that are either a result of cancer itself or related to cancer treatments. So I just wanted to highlight some challenging biopsies as this is one of the most important procedures that we do. Clearly it is difficult for Oncologist to treat patients in the absence of a diagnosis. That said,
cases such as this one should be easily doable for any experienced interventional list, and as you can see, this patient has confirmed metastatic adenocarcinoma.

So here is the second case, which I would say is much more challenging due to lack of any imaging finding on CT or ultrasound and you can see here it’s closed and you can see here it’s closed. Fortunately we were able to get adequate tissue sampling and help this patient get the appropriate chemotherapy that they needed to be on.
So I just wanted to discuss a couple of primary intra interventional oncology tumor therapies, both of which will be discussed in research by our trainees later in the session here we have two more guided ablation or tumor image guided tumor ablation, so the goals of Ablation is to eradicate all valuable malignant cells and stem spare normal surrounding tissues, treat tissues with unfavorable location or pattern of distribution for resection and or have multiple comorbidities. These are the most often used in
patients with low volume disease and required to bulking are typically done in an outpatient setting setting and these procedures are repeatable.

So if we can see here we have radiofrequency ablation and microwave which are heat based therapies. We have Cryo Ablation which is a coal based therapy and we actually have irreversible electroporation which is really to electrocute the tumors. Believe it or not, by changing the ionic potentials between the membranes. So ablation of liver tumors, which is in this was its initial indication,
This is 1 case of a patient with HTC that needed ablation as a bridge to transplant. As we can see, 2 1/2 years later, no tumor recurrence or any residual disease. Next was the case of an isolated colorectal liver metastasis. Who here you see a pet positive or hypermetabolic lesion in the right lobe of the liver who was successfully treated with Ablation and his team are free at one year?
instead of having a liver lesion, has a lung nodule. Here we can see that based on having heat based thermal ablation, the patient did very well at seven months. As you can see, there’s no residual tumor on the image Ng, and there was no local recurrence seen at three years. We can also treat bone metastasis. This is a patient with metastatic breast carcinoma with a focal right femoral and right hip pain limiting mobility for whatever reason, she refused radiation therapy and was treated with heat based thermal ablation and Samantha.
plasty is shown here and she had an immediate improvement in right femoral pain from 8 to 10 out of 10. This is a very interesting use of thermal ablation in this case, with cryoablation. This patient had metastatic Rectal Squamous Cell Carcinoma who had severe intractable 10 out of 10 pain, secondary to inoperable tumor recurrence infringing on the sacral nerve roots. She was successfully treated with partial cryo ablation of the bowel wall and you can see right here the low density ice she had immediate
or should say complete resolution of her pain within about 3 days. So she had actually no. Team up until a year, at which time she actually died and then Lastly we were able to treat this liver tumor here. That was a budding the left hepatic bile duct. We also have more regional therapies such as transarterial embolization. which is technically a non thermal ablation. So about nine months later the patient has no residual disease or recurrence. We also have more regional therapies such as transarterial embolization.
In these cases are typically reserved for patients with higher tumor burdens or are in neoadjuvant settings, or in cases where resection or ablation is in a location considered terribly difficult or dangerous.

We see a case of a patient with HIV, cirrhosis and a 4.8 centimeters segment. HTC Embolization was performed to maintain the patient on the transplant waiting list.

We see completing the Krosis, and she alternately underwent a transplant.

This is a patient with compensated HTP, sarot sis, Anna Sala,
Terry HTC and segment 8 and a platelet
NOTE Confidence: 0.80972403
count of 57 who also needs treatment.
NOTE Confidence: 0.80972403
There’s a bridge to transplant.
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This tumor is shown here is in
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a very difficult location,
NOTE Confidence: 0.80972403
and she successfully underwent
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embolization with no residual tumor,
NOTE Confidence: 0.80972403
and this patient also underwent
NOTE Confidence: 0.80972403
liver transplantation.
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Here we’re able to see a patient that was
NOTE Confidence: 0.8185584
treated in their 90s who has a large HTC.
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In this case, the ACC actually
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ruptured through the capsule,
NOTE Confidence: 0.8185584
and as you probably are all aware,
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this is associated with poor, if not dismal,
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 prognosis were able to successfully
treat it with radio embolization, which was done as an outpatient, and this can be seen here. She had complete response and lived up to five after four years later, and then Lastly. This is a case of a patient that has BI lo or HTC with extensive portal vein tumor. Rambus, so typically this patient would have less than six months to live, but as expected, this is a relatively young patient with the family, small young children, etc. So we try to offer procedure to help this patient and we did Chemoembolization.
and Fortunately we were successful in prolonging his life for about 16 months.

So to wrap up, I just want to give you my five year of vision for a modern academic evidence based intervention on college program.

First we want to increase the clinical research programs throughout the Smilow Cancer Hospital and Kiss Centers throughout the area.

Further, it will be important to improve the education for the community provider of the procedures that we offer and which patients are more likely to benefit.

We also need better integration of care.
into current and future oncology workflows.

We will be working on initiating some new clinical trials related to liver oncology.

As discussed last week on liver generation was, which was dragging one study, but we also are going to be involved in the leap 012 study, which is going to be an immunotherapy chemo embolization plus or minus immunotherapy that we're going to be initiating or starting very soon.

And then it's also going to be critical to have faculty who are sub specialized to be able to
provide this level of advanced air.

We also plan to make image guided biopsies more readily available and hoping to improve turn around time. There have been ongoing discussions with Doctor Chen Lu as you all know is the chair of pathology. To work on by an image guided by over Pozza Tori. As will be seen from the next speakers, we are currently working on advanced preclinical and Translational research with a focus on molecular imaging immuno oncology. We’re also very active in machine learning and artificial intelligence as
it relates to liver cancer and based on these interesting topics we hope to be able to achieve and expand our funding. And Lastly we have a newly established IR residency program. In this we would like to develop an Interventional Oncology Fellowship and we are looking into the possibility of applying for a T32 training grants. So with that, these are visions and goals I’d like to then introduce my Co director for the Interventional Oncology Research Lab at Yale, who will be discussing.
quantitative biomarkers,
molecular imaging in artificial intelligence
to guide the therapy of liver cancer.
So thank you for your attention.
Alright, thank you very much everyone.
I’m really excited to be presenting this
topic on behalf of our lab and this is
more of a vision presentation of what we’ve
accomplished and a couple of thoughts
that we put together over the last years.
None of this would have been possible without
really vast infrastructure of collaborators,
which I’ll be talking about
a little bit later.
I want to say that I very excited about.
David joining the group here and really being
our new leader and Interventional Ecology, and we all completely subscribed to the vision that she just provided. So as you know, I’m going to be focusing on the liver cancer, and primarily I’m going to start off with a BC else staging system. The most recent one was released in 2018, and even in that more recent addition to it we have seen a clear separation between intermediate station advanced stage disease, so they exist. Apparently in two separate planets, however, really in clinical practice and in signs,
00:14:43.830 --> 00:14:45.860 this is very transitional area where both
NOTE Confidence: 0.8774969
00:14:45.860 --> 00:14:48.398 seemed to be interacting quite extensively.
NOTE Confidence: 0.8774969
00:14:48.400 --> 00:14:50.703 We saw a lot of clinical trials
NOTE Confidence: 0.8774969
00:14:50.703 --> 00:14:52.978 focusing an overlap of those therapies,
NOTE Confidence: 0.8774969
00:14:52.980 --> 00:14:55.311 and this is exactly the realm where
NOTE Confidence: 0.8774969
00:14:55.311 --> 00:14:57.026 most patients are being diagnosed
NOTE Confidence: 0.8774969
00:14:57.026 --> 00:14:59.308 and also the realm where you know
NOTE Confidence: 0.8774969
00:14:59.308 --> 00:15:02.004 we think there is most room of
NOTE Confidence: 0.8774969
00:15:02.004 --> 00:15:03.536 improvement for patient outcomes,
NOTE Confidence: 0.8774969
00:15:03.540 --> 00:15:05.628 so systemic therapies for HTC then
NOTE Confidence: 0.8774969
00:15:05.628 --> 00:15:08.130 and now I borrowed the slides for
NOTE Confidence: 0.8774969
00:15:08.130 --> 00:15:09.896 from Agusan Abou Alfa, who’s?
NOTE Confidence: 0.8774969
00:15:09.896 --> 00:15:11.776 Medical Oncologist at Memorial Sloan
NOTE Confidence: 0.8774969
00:15:11.776 --> 00:15:14.690 and this is how the market look like.
NOTE Confidence: 0.8774969
00:15:14.690 --> 00:15:17.082 Five years ago we just had one drug
NOTE Confidence: 0.8774969
00:15:17.082 --> 00:15:19.790 and this it’s not even a complete view.
This is where we are right now.

So with him just five years, we have so many drugs being approved and most of ’em actually are very dedicated, specific targeted molecules and checkpoint inhibitors. So this flood of novel agents actually probably means the left ship of systemic therapy in the CL. See staging system and what we will witness is a greater overlap between local, regional and. Systemic therapies of immunotherapy. And this is where we come from.

We focused now on the biomolecular mechanisms.
in the tumor micro environment behind those therapies and their combination. So we focus on two of the well known hallmarks of cancer that are particularly relevant for HTC specifically on its ability to avoid immune destruction and the deregulation of seller energetic into metabolic phenotype. So let’s have a look at the HTC cell, so we now it has a very pronounced Warburg effect, and this is specifically a cell that is extremely dependent on the glucose metabolism. And so called the Arabic and anaerobic glycolysis, and well,
the glucose is being taken up with that sell.

It produces lactate.

It is that essentially is D Cup from the Krebs cycle, and this lacked.

It is then being flooded directly into the extra seller micro environment.

And because of that there was dramatic acid ification of the surrounding tumor micro environment.

And what does that really mean for us? The extracellular pH and liver cancer, especially aggressive age species known to be very, very low.

And now finding say that this is a very
important exclusion mechanism for four.

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Immune cells and the mechanism

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So this has been previously reported

NOTE Confidence: 0.8167382

and we now know more than ever that

NOTE Confidence: 0.8167382

actually tumor infiltrating T lymphocytes

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depend extremely on extra seller acidity

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and competitive glucose deprivation,

NOTE Confidence: 0.8167382

and the reversal of this hostile

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tumor micro environment can actually

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improve their infiltration into the tumor.

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An immune response.

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So to sum it up,

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loads for seller pH is a marker of

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tumor aggressiveness and the presence

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of Protons and lactate really protects
cancer against an immune response.

It promotes new angiogenesis.

The lactic acidosis plays a multifaceted role that is not fully understood for all variable immune cell subgroups, and the high lactic levels are actually strong predictors of metastatic disease and poor outcome.

So where does all this fit in with taste?

So theoretically this is an embolus therapy that changes the tumor micro environment. And what happens is that in theory tastes me potentially exacerbate a hostile tumor micro environment that attenuates treatment efficacy.
Let’s look at it.

I mean, it induces a hypoxic injury that potentially may exacerbate the low pH even further. It potentially stimulates brand eugenic signaling and the embolization even might prevent delected transport away from the tumor. So postdates tumor marker environment was thought to be immune inhibitory, but is that really true? I mean, let’s look at HTC in general, where it stands in terms of Genomic somatic mutations as opposed to Melanoma and lung cancer.
Really, HTC is somewhere in the middle, so the idea of the Immuno and inoculation with locoregional therapies was initially discarded because of that. However, let’s have a look at the pathology of a tumor treated with taste. This is a patient with HTC. Histology was taken 11 days post locoregional therapies that was transplantation. What we see in necrotic tumor packed with this particular case drug eluting beads. And surrounding that we see a very
dense immune infiltrate and if we zoom in we really almost see a secondary immune follicles and macrophages and T cells really accumulating the transitional zone. But they can’t really penetrate into the necrotic areas of the tumor where all the good end to Jenison. Why is that? So our mission was at this point to really look at the underlying mechanisms and how do systemic therapies interact? How does in the immune system and local regional therapies interact? So we wanted to develop imaging instruments for noninvasive functional
characterization monitoring of the tumor micro environment in the setting of the immune response and taste, and that was the mission of the lab that we essentially started several years ago. So the one of the first projects that I’m going to talk about is recently published paper clinical Cancer Research. That focused on the development of an extracellular pH probe that demonstrates extracellular pH noninvasively using spectroscopic methodology, and I’m actually really appreciate it. ’cause that partnered in design and
work on this novel mechanism with Daniel Komen and if I meet higher from the Mr Research Center who have been really instrumental and great partners in developing.

And we used to model of a rabbit liver tumor, which is so far the only moderate size animal model that has a faithful reproduction. Reproduction of an HTC tumor environment and the has a high clinical relevance because we can do the embolization also image those animals in real size clinical scanners.

We do have a 3T MRI system for that and also cutting edge IR suite which we use in the white Rick with the help
and support of Alston is this group. So this is an immuno competent host. Anna hyper glycolytic metabolic phenotype. An essentially those tumors have been characterized previously, is very reminiscent of the actual tumor marker environment of HTC. So what is a good way to image pH so their sensor jeans that you can use their luminescent probes that you can translate yourselves with reporters? But what we in radiology aim for is really the noninvasive measurement affects your seller pH and this is where our msit based spectroscopic
00:20:58.445 --> 00:21:00.545 birds methodology comes into place.
NOTE Confidence: 0.8162481
00:21:00.550 --> 00:21:02.435 This has been established previously
NOTE Confidence: 0.8162481
00:21:02.435 --> 00:21:04.320 in brain tumors by Daniel.
NOTE Confidence: 0.8162481
00:21:04.320 --> 00:21:05.955 And we have translated this
NOTE Confidence: 0.8162481
00:21:05.955 --> 00:21:06.936 essentially to deliver.
NOTE Confidence: 0.8162481
00:21:06.940 --> 00:21:08.296 This is NMR Spectra,
NOTE Confidence: 0.8162481
00:21:08.296 --> 00:21:09.991 scopic method that measures the
NOTE Confidence: 0.8162481
00:21:09.991 --> 00:21:11.609 redundant deviation of shifts and
NOTE Confidence: 0.8162481
00:21:11.609 --> 00:21:13.830 temperature in the region of the tumor,
NOTE Confidence: 0.8162481
00:21:13.830 --> 00:21:15.706 and we can generate the 3D extracellular
NOTE Confidence: 0.8162481
00:21:15.706 --> 00:21:17.975 pH map that provides us with essentially
NOTE Confidence: 0.8162481
00:21:17.975 --> 00:21:19.379 a very accurate characterization
NOTE Confidence: 0.8162481
NOTE Confidence: 0.8162481
00:21:21.380 --> 00:21:23.702 So if we look at the tumor in by
NOTE Confidence: 0.8162481
00:21:23.702 --> 00:21:25.981 itself and measure it as compared
NOTE Confidence: 0.8162481
00:21:25.981 --> 00:21:27.931 to the surrounding liver tissue,
we see that the tumor is by itself has much lower pH and baseline in an untreated fashion and the surrounding liver, and that’s important. And we know that this is probably due to the overt Warburg effect and overexpression of glued one and lamb two as indicators for the micro environment. Now, what does taste actually do with it? And this is where the surprising result from our study came in. We looked at the effects of embolization with little one day, one week, and two weeks after we actually
treat those tumors and measured the pH and as opposed to most of the assumptions that taste is going to actually exacerbate the The Anti. Yeah, I mean the logic, the immune, evasive tumor micro environment, it actually did the opposite. So what we see is a normalization of the tumor pH towards almost delivered background levels. Overtime after taste. And that is an important finding because that gives us an opportunity to use local regional therapy in preparation for successful anti checkpoint inhibition.
therapy and we actually demonstrated this also with a more direct and exacerbated model. Where we.

Eustace and actually injected bicarbonate directly with taste and what we demonstrated here is that on baseline you have an acidic tumor with taste. You have a minor improvement of pH towards normal over overnight essentially, but if you add bicarb you can immediately improve the pH almost essentially to normal and yellow and green means higher levels than blue. If we now look at, for example, H Lady are expression at baseline,
we see immune cell exclusion were really see
all the immune cells in the tumor periphery.
And with with taste alone,
immediately at least one day after therapy,
you don’t really see a lot of immune invasion,
but with taste and bicarb,
basically improving and elevating a pH,
you see massive intratumoral infiltration of immune cells,
and that’s an important finding that we made here in actually an important other thought that we should be thinking about as a group generally in oncology, and what kind of agents we use.
So when we use a key mobilization with oil,
which is Lupito, we achieved, achieves seemed to be achieving very different effects. Compared to, for example, using an cuisine beads or Lumi beads, which is another flavor of beads and that is important for us to understand because through the uncle logic community taste was taste for long period of time, but in reality it is not because we know that different embolic particles will induce very different in a logical effects in very different changes
to the tumor marker environment.
And that is something that we really need to study, especially if we want to combine the local regional therapies with systemic therapies and checkpoint inhibition.
Now another level of investigation that we took to token published recently in radiology, again close collaboration with Daniel Komen Fahmideh Hyder but also other groups like rip Ocala’s group and also want to mention Ruth, and Joshi, who helped us generate this research.
Here we wanted to demonstrate that we can actually use molecular dedicated inmar probes nanoprobes labeled antibodies to visualize the immune system surrounding those tumors in vivo and noninvasively. So what we did is we use both iron oxide particles and the direct injection of gadolinium labeled antibodies to visualize those tumors and put those animals with those implanted tumors into them are what we demonstrated was that we were able to clearly delineate microfusion immune cell infiltration and macrophage.
and immune cell accumulation in the periphery of those tumors.

On T2 MRI sequences, and that was proven in histologically with Prussian blue staining, which stands for iron.

And we saw that the spines, the iron oxide particles really deposited and CD11B positive macrophages confirmed that later with CD 68 staining and the same thing is true for our induction injection of gadolinium labeled antibodies.

You probably heard about this from the molecular imaging using PET, but here we have a much
higher focal resolution where we label antibodies with gadolinium and then inject them directly into those tumors and through the artery, and we can see that there is very specific accumulation and staining. Of immune cells and perforate the tumor that we can now really localize characterize, and that’s that’s a big step forward because not only can we now image the tumor marker environment from a pH perspective, we can also images from a presence and functionality of immune cells. So for the first part of the conclusions are their appearance of, for example,
more than five targeted agents to treat HTC will cause a left shift of systemic therapy in the BC else, and we really must do some heavy lifting. It’s up to art actually to put the collaboration between the Interventional in college and Immuno Oncology on the right track. From a science perspective we must also work more on non invasive imaging modalities and we did so with the extracellular pH that revealed that ace actually is an inducer. Profound changes to tumor marker environment that may help immunotherapy to be more effective,
and pH is key for us as marker, but the changes in pH depends on the embolic materials that we use. We also now know that C test would lipiodol may achieve a partial reversal of the immune evasive tumor marker environment on itself two weeks after taste, and that we can use them are instruments to actually detect immune cells directly surrounding the tumor. So in summary, the for the first part of my conclusion is that local regional therapy is that local regional therapy and intervention alone college. You must be established in combination.
with each other.

We have to have a synergy between the two iOS interventional and Immuno Oncology and it’s up to us to work on that. And that generates another bigger problem that we really workup on very closely with Jim Duncan and collaboration with that group and biomedical engineering. And this is the overwhelming growth of data and will be talking about this little bit later. Tall is going to be presenting on that, so we know that the data that we have specifically in imaging and. Cancer in general explode so we have more than 20 times more data.
00:27:42.828 --> 00:27:44.664 today than we have in 2013,

00:27:44.670 --> 00:27:47.428 and so that is a huge challenge.

00:27:47.430 --> 00:27:49.240 Anne, it’s David already presented.

00:27:49.240 --> 00:27:50.684 We have different flavors

00:27:50.684 --> 00:27:51.767 of chemo embolization,

00:27:51.770 --> 00:27:53.218 embolization with drug alluding

00:27:53.218 --> 00:27:54.304 Beatson Radio mobilization.

00:27:54.310 --> 00:27:56.356 We have a variety of different

00:27:56.356 --> 00:27:58.178 methodologies in ways how we

00:27:58.178 --> 00:28:00.370 can introduce tumor necrosis,

00:28:00.370 --> 00:28:02.575 cold heat,

00:28:02.575 --> 00:28:04.583 and electrocution in a way we have

00:28:04.583 --> 00:28:06.613 five different and more coming

00:28:06.620 --> 00:28:08.540 all of which pose different changes

NOTE Confidence: 0.81775826
to the tumor micro environment.
So we went overwhelming burden of complex data that actually may impede effective clinical practice. We need to address that.
And so, how do we transform the data from burden to value?
We know that we have an increase in data. We have very complex medical health records. We have genomics sequencing information. We have the availability of complex computer based algorithms and now the availability, availability of computational power at a lower cost. And that is the space where
artificial intelligence now comes in. And this is essentially data driven. Learning that deep down can be explained as machine learning that recognizes trends and objects in pre labeled patterns or deep learning, and that may hopefully increase the workflow efficiency, improve our diagnostic accuracy really enabled predictive recommendations.
Therapeutic recommendations and help introduce Precision Medicine, but caution is still very important and AI is being hyped and I think we need to approach it in a gradual fashion. Really see what is doable and what’s not. So how can this advanced data analysis help us? It can improve the diagnosis from automation and introduction of novel biomarkers. It can also help us make therapeutic decisions and probably introduce a level of better personalized care. Hopefully we will be able to ultimately improve interprocedural guidance, especially with now with the
introduction of robotics into IR, and specifically follow up imaging.

We hope that in the realm of tumor response and patient outcome prediction directly after the therapies, those technologies will help us put all this data together.

Now, prior to introducing the other speakers and talking and giving specific abstract presentations.

The two larger topics that I presented. I want to really thank the sources of funding inspiration mentoring in our community. Already mentioned Drake.
I wanted to thank Jim sincerely and Todd and David who joined the lab. Also great partners of mine are Ruth and Nick and I really appreciate those collaborations that are increasingly interdisciplinary, but at the same time I wanted to also point out that mean radiology have a very large biomedical imaging collaborative network, and I want to thank from Eden, Daniel, and Larry and everyone mentioned here. From White Rick, who have been instrumental over the last five years in my personal development.
and also in the development of the lab, and I think that is the environment that we need and we need to highlight to the Cancer Center and introduce it to all of you. And I’m very happy to do so here. And, you know, there’s one thing across all this. There is a single light of science.
then to brighten it anyways.

This is our group model by Isaac Asimov.

And with that, I'd like to introduce two or

Jessica Santana. She’s going to be talking about

taking the molecular imaging really to next level in our new

animal models, and talk is going to be

talking about his role as Biomedical Engineering graduate student within

the biomedical imaging Sciences on

focusing on predicting outcome and
00:31:29.743 --> 00:31:31.940 recurrence of HTC after intervention.

00:31:31.940 --> 00:31:33.700 And I'd like to.

00:31:33.700 --> 00:31:35.386 And now the stop sharing the screen and give it to Jessica.

00:31:45.710 --> 00:31:47.226 Hi all, I'm Jessica.

00:31:47.226 --> 00:31:49.500 I am a master level demonologist

00:31:49.574 --> 00:31:51.864 Anna graduate student at the Yale Interventional College Lab

00:31:51.864 --> 00:31:56.130 and I'm very excited today to be presenting my work, titled,

00:31:56.130 --> 00:31:58.092 Noninvasive molecular imaging

00:31:58.092 --> 00:32:01.116 allows characterization of the immune response following hepatic radiofrequency Ablation in a mouse model.

00:32:07.350 --> 00:32:08.416 Nothing to disclose,
So giving you a brief overview on hepatocellular carcinoma.

So as we know, this is a classical inflammation associated Carcinoma and now is the third most common cause of cancer related death worldwide. With the majority of patients being treated with locoregional therapy as they may alternative option over surgery. However, the problem with locoregional therapy is that a significant fraction of patients they tend to recur and the causes for recurrence can vary a lot. And it has been suggested, for example, that the immune response to radiofrequency ablation can play both roles.
An Protogenic Side effects as well as abscopal effects that in turn can positively impact the immune response to cancer. However, we have currently no instruments that would allow us to non invasively monitor such immune response. So the purpose of this work is to develop a noninvasive molecular imaging instruments to visualize such immune response to thermal injury following RFA. So our group has built a translation of mouse model of radiofrequency ablation as a platform to develop and validate mirbase dimona probes for in
vivo imaging of the immune system. And based on our findings, we have observed that there is a after radiofrequency ablation and normal liver. There is a strong time dependent local infiltration of immune cells that orchestrates the tissue healing process and there is an overtime transitional zone of those immune cell infiltrate. So having a specific cell population locally present at the transitional zone between the necrotic area and the normal liver parenchyma at a specific time point serves us as an illegal platform to build and validate our dedicated immune probes.
So guiding you through our experimental design.

We have a bladed and normal liver of a mouse, and after characterizing a large infiltration of a specific cell population is specific time point.

We have established a dedicated gadolinium labeled antibody that was delivered systemically to target a specific cell population at the chosen time point Post Ablation.

And a second immune probe also used in this study, is the small iron oxide particles, and we know that RN particles they...
have been largely used in the clinical setting as the dark contrast agent and once they are delivered systemically, they are able to be phagocytosed by circulating phagocytes that once they migrate to the site of inflammation they can cause a local deposition. In this study we have demonstrated that both gadolinium labeled antibodies inspire probes. They were able to be imaged using a higher resolution Mr animal scanner. So in our first setting of experiments we have demonstrated that the ablation zone itself can be easily imaged on a 9.4 Tesla Burger.
So here on your left you have the pictures taken seconds after ablation to show you or give you an idea of how the ablation site looks like an one week post Ablation, and we have delivered pure gadolinium systemically and we ran a T1 weighted MRI sequence and we could see precisely the Ablation. Side and on your right we have an ex vivo confirmation of what we see on them, but you might have been wondering why exactly 7 days post ablation. So to the best of our knowledge,
we know that our thing doost thermal tissue injury, largely contributes to a strong time dependent innate immune response at the margins of the necrotic zone. And according to our findings, we have observed the largest accumulation of city 68 positive macrophages in the transitional zone, precisely seven days post ablation. So this is the time point we decided to base our experiments on. So we have decided to deliver systemically. Those aren’t oxide particles. Seven days post Ablation and we have confirmed that there is a local
deposition of those iron oxide particles exactly 24 hours after systemic delivery. At the transitional zone. So here we have an ex Vivo Prussian blue staining, although one week post ablation, mouse liver 24 hours after systemic delivery of Spions and when we image those animals, we could demonstrate any Viva local deposition of those phagocytes at the transitional zone. So here on your left you have a teacher weighted MRI of a one week post Ablation, 24 hours after systemic delivery
Note: Confidence: 0.77417207

Spions and as a Redpath

NOTE Confidence: 0.77417207

00:37:02.857 --> 00:37:05.395 correlation we confirm the ex vivo
NOTE Confidence: 0.77417207

00:37:05.395 --> 00:37:07.360 specifically position of the spine.
NOTE Confidence: 0.77417207

At the transitional zone,

NOTE Confidence: 0.77417207

00:37:08.900 --> 00:37:10.440 3 min inflorescence and
NOTE Confidence: 0.77417207

00:37:10.440 --> 00:37:11.830 Prussian blue staining.
NOTE Confidence: 0.7773221

And As for our gadolinium based
NOTE Confidence: 0.7773221

00:37:16.600 --> 00:37:19.460 immuno probes, we have used a anti CD
NOTE Confidence: 0.7773221

00:37:19.460 --> 00:37:21.740 68 antibody tagged with gadolinium.
NOTE Confidence: 0.7773221

00:37:21.740 --> 00:37:24.351 So after XP will observing a massive
NOTE Confidence: 0.7773221

00:37:24.351 --> 00:37:26.361 infiltration of city 60 positive
NOTE Confidence: 0.7773221

00:37:26.361 --> 00:37:28.421 macrophages in the prohibition of
NOTE Confidence: 0.7773221

00:37:28.421 --> 00:37:30.499 zone we delivered gadolinium tagged
NOTE Confidence: 0.7773221

00:37:30.499 --> 00:37:32.815 with city 68 systemically and was
NOTE Confidence: 0.7773221

00:37:32.815 --> 00:37:35.665 able to see a specific position of
NOTE Confidence: 0.7773221

00:37:35.665 --> 00:37:38.330 those cells in the Prohibition of rim.
So here on your left you have the Ablation. Cite the picture taking seconds after ablation showing the ablation site. And we also have 81 way to MRI when we post Ablation After 24 hours with gadolinium city 68 delivered systemically. And on your left you have the picture taken, ex Vivo confirming of what we’re seeing on the MRI. And to confirm that this parable itional darkroom is seen precisely in animals receiving those city, 68 tagged to 68 antibodies tagged with gadolinium. We also ran T1 weighted MRI with
00:38:23.155 --> 00:38:24.325 pure gadolinium.
NOTE Confidence: 0.7773221
00:38:24.330 --> 00:38:27.434 So on your lap to have the baseline
NOTE Confidence: 0.7773221
00:38:27.434 --> 00:38:29.320 and it comparison,
NOTE Confidence: 0.7773221
00:38:29.320 --> 00:38:32.648 we have a T1 weighted MRI with pure
NOTE Confidence: 0.7773221
00:38:32.648 --> 00:38:35.454 gallium injected and we have confirmed
NOTE Confidence: 0.7773221
00:38:35.454 --> 00:38:38.286 that only with animals receiving city
NOTE Confidence: 0.7773221
00:38:38.373 --> 00:38:41.565 68 tagged with get alignment we have
NOTE Confidence: 0.7773221
00:38:41.565 --> 00:38:43.888 this precise parable itional rim
NOTE Confidence: 0.7773221
00:38:43.888 --> 00:38:46.732 showing a local infiltration of CD
NOTE Confidence: 0.7773221
00:38:46.732 --> 00:38:49.490 16 positive macrophages and therefore
NOTE Confidence: 0.7773221
00:38:49.490 --> 00:38:52.928 in vivo visualization of those cells.
NOTE Confidence: 0.7773221
00:38:52.930 --> 00:38:55.478 We have also confirmed the ex vivo
NOTE Confidence: 0.7773221
00:38:55.478 --> 00:38:57.808 a specific labeling of immune cells
NOTE Confidence: 0.7773221
00:38:57.808 --> 00:38:59.748 using imaging mass atama tree.
NOTE Confidence: 0.7773221
00:39:02.030 --> 00:39:04.094 So he ran on your left.
NOTE Confidence: 0.7773221
00:39:02.030 --> 00:39:04.094 We have the T1 weighted MRI of one
NOTE Confidence: 0.7773221
week post ablation after gadolinium labeled antibody administration, where you can see the rim of the local deposition of the infiltrating cells an on your right. We have the X visual confirmation with the image Ng Masama tree of local deposition of the sea to 68 macrophages. In the transitional zone. So as the main conclusions and findings of this study, it tells us that both spines and Catalina based molecular imaging allows for specific labeling of local immune infiltrate,
00:39:35.550 --> 00:39:37.734 and this is also a translation of
NOTE Confidence: 0.7773221
00:39:37.734 --> 00:39:39.834 study with the proof of principle
NOTE Confidence: 0.7773221
00:39:39.834 --> 00:39:42.382 for the visibility of the MRI imaging
NOTE Confidence: 0.7773221
00:39:42.455 --> 00:39:44.534 for of macrophages on a 9 point.
NOTE Confidence: 0.7773221
00:39:44.540 --> 00:39:46.236 For Tesla MRI scanners.
NOTE Confidence: 0.7773221
00:39:46.236 --> 00:39:48.780 And also tells us that noninvasive
NOTE Confidence: 0.7773221
00:39:48.858 --> 00:39:51.228 in vivo detection of the immune
NOTE Confidence: 0.7773221
00:39:51.228 --> 00:39:53.433 system can be achieved using
NOTE Confidence: 0.7773221
00:39:53.433 --> 00:39:55.080 dedicated immune probes.
NOTE Confidence: 0.7773221
00:39:55.080 --> 00:40:00.390 An ask for our future perspective
NOTE Confidence: 0.7773221
00:40:00.390 --> 00:40:03.117 and clinical application.
NOTE Confidence: 0.7773221
00:40:03.117 --> 00:40:05.512 We can have this as a useful tool to
NOTE Confidence: 0.7773221
00:40:05.512 --> 00:40:08.037 study and characterize the interplay
NOTE Confidence: 0.7773221
00:40:08.037 --> 00:40:10.559 between the tumor micro environment
NOTE Confidence: 0.7773221
00:40:10.559 --> 00:40:13.310 and the cell opinion selectivity in
NOTE Confidence: 0.7773221
00:40:13.310 --> 00:40:16.608 vivo and also gives us the possibility
to integrate complimentary molecular MRI imaging of the immune system. And let’s say the extrasolar pH liver cancer model for simultaneous characterization of this immuno metabolic cross dock. This also serves us as a platform to study strategies for local modulation of the immune microenvironment towards a moon are permissive phenotype and can also serves us as if they were gnostic immunotherapy. So I’d like to thank you for the opportunity to present this work as well as the yield biomedical
imaging Department. And now I’ll give you the word to my friend, tall.

Hello everyone, my name is Charles early and I’m graduate student in the Biomedical Engineering program here at Yale and I’m a member of the Interventional Oncology lab since 2018 and today I’m going to be presenting our project on deep learning use to predict disease recurrence of HTC, based on NMR imaging.

So a little bit about ATC, so HTC is the primary tumor of delivered. It usually develops in the setting of chronic liver disease, and while the diagnosis of ATC...
could be made by imaging alone, sometimes a biopsy may be required to support this diagnosis. A little bit statistics every 40 seconds at patient diagnosed with ATC in 2020 alone, the death rate is approximately the 800,000 deaths worldwide. ATC may recur and there is no significant imaging biomarker or clinical biomarkers to reliably predict recurrence before location to treatment. One of the treatment is liver transplantation. It helps to decrease the chance of disease recurrence.
However, we are all aware to the shortness of organs. Therefore, 2 criteria of allocations of levers are being used. One of them is the Milan criteria, which was presented in 1996 and the other one was presented by the University of California, San Francisco on 2001 basically extended this Milan criteria. Both of them are based on low level handcrafted features such as tumor size and number of tumors. Using these criteria, we are seeing 15 to 20% of transplanted...
patient to occur within the 1st five years.

So as I said, these two criteria have suffered from false positives, and our hypothesis is that there is more information in radiological images, specifically MRI that correlate with HTC recurrence. Then the naked eye could detect and the way we’re going to try to test this hypothesis is by using deep learning algorithm to extract features from MRI images and try to use them to correlate to ATC recurrence. And a little bit before I start
00:43:22.083 --> 00:43:23.720 talking about our methodology,
NOTE Confidence: 0.82661027
00:43:23.720 --> 00:43:25.814 I will talk about data
NOTE Confidence: 0.82661027
00:43:25.814 --> 00:43:27.210 driven predictive modeling and
NOTE Confidence: 0.82661027
00:43:27.273 --> 00:43:29.049 a little bit of deep learning.
NOTE Confidence: 0.82661027
00:43:29.050 --> 00:43:31.048 So when we talk about data
NOTE Confidence: 0.82661027
00:43:31.048 --> 00:43:32.047 driven predictive model,
NOTE Confidence: 0.82661027
00:43:32.050 --> 00:43:34.374 we usually refer to two different variables,
NOTE Confidence: 0.82661027
00:43:34.380 --> 00:43:36.100 the Explanatory variable and explain
NOTE Confidence: 0.82661027
00:43:36.100 --> 00:43:38.866 part of our target and we want to
NOTE Confidence: 0.82661027
00:43:38.866 --> 00:43:40.174 take these explanatory variables
NOTE Confidence: 0.82661027
00:43:40.174 --> 00:43:42.160 to feed them into predicted model
NOTE Confidence: 0.82661027
00:43:42.160 --> 00:43:44.365 which will give up the outcome of
NOTE Confidence: 0.82661027
00:43:44.370 --> 00:43:46.035 our target building which could
NOTE Confidence: 0.82661027
00:43:46.035 --> 00:43:47.367 be recurrent or not.
NOTE Confidence: 0.82661027
00:43:47.370 --> 00:43:48.842 And this predictive models
NOTE Confidence: 0.82661027
00:43:48.842 --> 00:43:49.946 has different shapes.
And algorithms which you may hurt. For example your networks this season.

Trees as VM’s. All in all, these algorithms that try to do the same thing they try to create or to estimate a mathematical function that correlated this input into doubt.

And there are two main elements of this estimation process. One of them were trying to see what is the mathematical element interaction between our features and the mathematical operations. That’s going to be incorporated.
within these mathematical function.

For example, the multiplication of X1 and X2 and the second thing we're trying to estimate the weight of these mathematical elements within this function, which could be seen here as better 0, better one, etc. And I'll give a short and very simplistic example of these data driven predicted model.

So here we are, having having only one variable Explanatory Variable, which is the age and we are trying to predict the disease patient trying to predict the disease patient is positive or negative to the disease.
So for example in the right side of the screen you can see this mathematical function. Why would be considered positive if the age is greater than better otherwise negative? And as we get more and more examples we could. For example, here we are estimating better to be 60, but as more data comes we can update modifier. Wait and basically change our function. Ann everything is OK till we have a data example that prevent us from.
creating one to use this mathematical function to a separate between these these two groups.

So here we need to incorporate a new feature, for example wait when we are doing that.

We can create a more complex function to separate these two groups and basically this is what we’re going to try to do.

Today we’re going to try to find the features that will allow us to separate between the recurrence in Nonrecurring.

When we’re talking about deep learning where basically usually refer to neural networks, and you run networks is again an algorithm that allows us to approximate...
almost any mathematical function that correlate input into output, and it does that by finding interaction between features. Convolutional neural network allow us to search for petitive patterns within an image and then correlate them to the output variable so it tries to find high level features such as edges and the more deeper we go, the more complex the feature become and allow us to separate between the groups that were trying to suffer. A little bit of our data, so we had 120 patients 18 years old or older,
88 minutes and 32 females.

All of them were diagnosed with HTC between 2005 to 2018.

So the patient went into MRI imaging, then were diagnosed with HTC and then got treatment 29 oblations, 32 receptions and 5:59 presentations.

An time went by, some of them recur, and some of them stop their follow which we considered to be non recurrences.

To this time that I can call time

To recurrence and this would be our explained variable,

the variable that we’re going to try to predict.

With respect to our input data,
we’re going to use conference enhanced multi phase liver magnetic resonance imaging, and we’re going to use three different phases that the arterial, the portal venous and the delay. So the question that we’re trying to answer here is can we predict ATC recurrence using pretreatment MRI images? In other words, are they visual features in free treatment MRI that correlate with HTC disease recurrence? So to visualize that we’re going to use the input MRI input data as an input data to freedom into.
a predictive model which will be convolution on your network and to predict whether the patient will reoccur within one year two years after six years after treatment.

So here are the results. Here we can see the results for these 6 * 6 timeframe. So one year for occurrence, two years of free France up to 6, zero for occurrence and this figure present the relationship between the true positive rate to the false positive rate on our test cohort and seeing these 45% curve, which represents basically
a random chance to predict, we can see that all of our curves is above that. Which means that our model has prediction power.

Another analysis that we did was to try to use Kaplan Meier curves and our predictions to separate our cohort into risk groups. Soloist group to recurrence in high risk to recurrence and we got significant results for your current free survival for four out of the six times you can here, you can see the six different figures.
each for one time for each time frame.

So to summarize,

the current state of the art criteria

based on low level handcrafted

radiological features such as tumor size,

number of tumors and this study

showed that there are still unknown

visual features in pretreatment.

MRI does correlate with recurrence of ATC.

Secondly,

the current state of the art selection

criteria suffers from false positives

and we showed by incorporating

machine learning based algorithms

we could potentially improve the

prediction of AGC recurrence.
Little bit of limitations and future research.

We used a single site cohort from Yale Hospital, which was small 120 patient, which has the limitation of generalize the results for other sites and therefore will need to increase our sample size or incorporating patient from different side.

And maybe single data modality, maybe not enough, so in future research we recommend to test interaction between imaging and clinical data,
00:50:11.460 --> 00:50:15.040 even incorporating more imaging modalities.
NOTE Confidence: 0.7972218
00:50:15.040 --> 00:50:15.988 Thank you very much.
NOTE Confidence: 0.8563696
00:50:23.210 --> 00:50:25.376 So, so that was really great.
NOTE Confidence: 0.8563696
00:50:25.380 --> 00:50:27.810 Hope you all were able to
NOTE Confidence: 0.8563696
00:50:27.810 --> 00:50:29.940 see what exciting work word.
NOTE Confidence: 0.8563696
00:50:29.940 --> 00:50:32.340 You know, doing in this lab?
NOTE Confidence: 0.8563696
00:50:32.340 --> 00:50:34.340 Does anybody have any questions?
NOTE Confidence: 0.83548236
00:50:35.410 --> 00:50:37.022 And individuals can certainly
NOTE Confidence: 0.83548236
00:50:37.022 --> 00:50:39.037 submit their questions on chat,
NOTE Confidence: 0.83548236
00:50:39.040 --> 00:50:41.176 but we did receive one which
NOTE Confidence: 0.83548236
00:50:41.176 --> 00:50:43.618 David you took the Liberty of
NOTE Confidence: 0.83548236
00:50:43.618 --> 00:50:45.490 at least answering online.
NOTE Confidence: 0.83548236
00:50:45.490 --> 00:50:48.706 But let me for the benefit of all.
NOTE Confidence: 0.83548236
00:50:48.710 --> 00:50:51.531 Let me just toss this out so
NOTE Confidence: 0.83548236
00:50:51.531 --> 00:50:53.730 Joseph Cam asked, you know,
NOTE Confidence: 0.83548236
00:50:53.730 --> 00:50:56.205 essentially, how do you decide?
On the specific procedure be RFA, thermal abrasion, ablation, cryoablation, and also relative to contraindications. How do you make those choices? Each ablation modality has its pros and cons, and clearly my goal for today was not to go into my own personal research and discuss a lot of this research and discuss a lot of this stuff in depth because I really wanted to highlight our trainees. But basically you know,
for liver it’s pretty much understood that heat ablation is actually what is preferred, and that’s because over the years well, first of all it’s very effective. But over the years, there’s been concerns with Cryo Ablation on what’s called something called Cryo shock. There’s questions about fracturing the liver. There’s no way of really cauterizing any bleed that you can do with microwave or RFA and a whole bunch of others. So it’s really the complications in this in this setting that makes it less ideal than four. For the Heat base, now the one positive thing is we
shown in some of the cases is that you do get the ice ball which has low density ice and that actually allows the operator to really sculpt the margins where you want to treat in other organs. Systems like the lung and kidney is really a dealer’s choice so that there have been papers on both. In terms of using cryoablation or heat ablation for those that were just involved in a study that was recently published in the Journal of thoracic oncology, which was a prospective clinical
00:53:04.080 --> 00:53:06.248 trial called solstice that.
NOTE Confidence: 0.83871114
00:53:06.250 --> 00:53:08.420 Did show benefits of cold,
NOTE Confidence: 0.83871114
00:53:08.420 --> 00:53:09.290 you know,
NOTE Confidence: 0.83871114
00:53:09.290 --> 00:53:12.335 for for lung nodules and then I
NOTE Confidence: 0.83871114
00:53:12.335 --> 00:53:14.910 already as I kind of explained,
NOTE Confidence: 0.83871114
00:53:14.910 --> 00:53:17.508 it’s kind of a niche application.
NOTE Confidence: 0.83871114
00:53:17.510 --> 00:53:19.562 Mostly used in pancreas,
NOTE Confidence: 0.83871114
00:53:19.562 --> 00:53:23.362 but it’s in an area where it’s
NOTE Confidence: 0.83871114
00:53:23.362 --> 00:53:25.210 difficult to treat.
NOTE Confidence: 0.83871114
00:53:25.210 --> 00:53:27.415 Areas which have vital structures
NOTE Confidence: 0.83871114
00:53:27.415 --> 00:53:28.738 in your body,
NOTE Confidence: 0.83871114
00:53:28.740 --> 00:53:31.386 so that’s the I guess summary
NOTE Confidence: 0.83871114
00:53:31.386 --> 00:53:33.150 of that so thanks.
NOTE Confidence: 0.8708769
00:53:35.320 --> 00:53:38.371 So let me ask a follow up question ’cause
NOTE Confidence: 0.8708769
00:53:38.371 --> 00:53:41.942 you great deal of the work is really
NOTE Confidence: 0.8708769
00:53:41.942 --> 00:53:44.390 advancing understanding the nature of

95
the immune infiltrate post procedure.

And Moreover, how to address how to make the environment more hospitable?

Two immune cells, Sony aspid,

be both with regard to the imaging techniques monitoring techniques and perhaps the introduction of bicarbonate.

How much you leverage all of this to think about combining these approaches with ongoing immunotherapy immuno therapies that are under development in HTC?

Right, I mean that’s a really important question that we’re actually trying to answer ourselves.

As David mentioned,
I mean, we're right now. Actually submitting one or an application after the other because we want to investigate exactly those points we generated. This preliminary data. Now we want to take it to the clinical perspective and do also clinical perspective and do also trials and immediate future. So I think there is a couple of limitations that we first need to address, and for the pH Image Ng, this is certainly the contrast agent, which is not done yet. Applied and in the human scenario, so we need to make sure that we
can do that safely, you know.

Secondly, I think you know the imaging of the immune system is a very hot topic and is being hotly discussed and worked up on both by the nuclear medicine community as well as you know us, and I think that both approaches have their merits in their drawbacks, and I think that this will definitely bring a breakthrough in terms of imaging biomarkers.

As we know in HC see only 20% of patients at Prof. Roundabout respond to immunotherapy.
But we treat a lot of them with it, and so we want to make sure we choose their right patients for the right therapy. And that's the whole goal. As for you, As for the real application of bicarb, that is an approach that could be translated into clinical trial very easily. I mean, bicarbonate is not a harmful substance. It could be used in just used in a clinical trial with taste, and I think we need to really think about using that as an addition and an additional.
Arm, possibly in one of the clinical trials that David is bringing on the board to use taste in combination with the immuno therapies. And I think that that would be a very simple initial fix. To do that. I mean there is very little Harmon. Probably you know some major benefit that we could get from that. So we need clinical trials in this respect and we need more translational contrast agent and more research.
00:56:13.661 --> 00:56:15.085 amazing infrastructure with RMR
NOTE Confidence: 0.85417795
00:56:15.085 --> 00:56:17.029 Research Center here and the Pet
NOTE Confidence: 0.85417795
00:56:17.029 --> 00:56:18.910 Center on the other hand 2.
NOTE Confidence: 0.85417795
00:56:18.910 --> 00:56:20.408 To actually do that kind of research.
NOTE Confidence: 0.8901477
00:56:21.330 --> 00:56:23.226 And so let me as a follow up.
NOTE Confidence: 0.8901477
00:56:23.230 --> 00:56:25.211 So let me ask, given what you’re
NOTE Confidence: 0.8901477
00:56:25.211 --> 00:56:27.308 describing in the nature of the immune.
NOTE Confidence: 0.8901477
00:56:27.310 --> 00:56:29.470 Response, immune environment,
NOTE Confidence: 0.8901477
00:56:29.470 --> 00:56:33.790 fear after procedures such as these.
NOTE Confidence: 0.8901477
00:56:33.790 --> 00:56:36.355 Desert potentially suggests that any
NOTE Confidence: 0.8901477
00:56:36.355 --> 00:56:40.048 efforts right now to combine a checkpoint
NOTE Confidence: 0.8901477
00:56:40.048 --> 00:56:43.174 inhibitor with taste or other ablation
NOTE Confidence: 0.8901477
00:56:43.174 --> 00:56:45.960 procedure may not be yet optimized.
NOTE Confidence: 0.8901477
00:56:45.960 --> 00:56:48.140 Turn to really achieve what we
NOTE Confidence: 0.8901477
00:56:48.140 --> 00:56:50.170 hope they would achieve because of
NOTE Confidence: 0.83878195
00:56:50.170 --> 00:56:52.276 the nature of the environment absolutely,
and this is exactly what I showed. If you remember one of the slides had different embolic agents, and so we’re using various symbolic agents, various agents. If we inject into the tumor, that may be pro or anti inflammatory. We then also combine taste and checkpoint inhibition in tumors that may be hot or immunologically cold. So essentially you know a lot of these trials will probably have very non significant results and probably will never achieve. Yeah, it is certain level of clinical
that we hope for.

Just because we don’t know what we’re doing.

Essentially so when we combine Interventional

in college and Immuno Oncology,

we just go about it and say one size

fits all and that is something that I

feel like is is the major key point

that we need to address and one of

these issues is that in Interventional

Ecology Community would just did not

have the academic culture and you

know research environment so far and

this is across multiple institutions

across our entire community.

To actually tackle those topics,

and I think now we as we more
00:57:54.822 --> 00:57:56.544 understand that our therapies are necessary in our increasingly combined with systemic therapy,
00:57:59.760 --> 00:58:01.410 we need to investigate that,
00:58:03.818 --> 00:58:05.370 have major breakthroughs in the next three to five years. Thank you.
00:58:07.662 --> 00:58:10.980 Well, I know where at the top of the hour, and I want to thank Jessica and tile
00:58:13.220 --> 00:58:15.223 and Julius and David for really a remarkably stimulating body
00:58:16.603 --> 00:58:19.116 of work and Bradley bring to our
00:58:21.255 --> 00:58:23.130 Interventional Onkologie So you know, thank you for this continued education
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for the great work you’re doing and everyone on line. Thank you.