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. Cancer Center in our University and health care system and you know, really focused on. 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 leader for today’s session. 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 lab vice chair for clinical 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
NOTE Confidence: 0.8278826
00:01:55.643 --> 00:01:57.689 management of colorectal liver metastases.
NOTE Confidence: 0.8278826
00:01:57.690 --> 00:01:59.510 Today’s session, as you stated it will
NOTE Confidence: 0.8278826
00:01:59.510 --> 00:02:01.549 be focused on Interventional oncology.
NOTE Confidence: 0.8278826
00:02:01.550 --> 00:02:04.262 What it is in some of the exciting
NOTE Confidence: 0.8278826
00:02:04.262 --> 00:02:06.678 research being done in our lab at Yale.
NOTE Confidence: 0.8278826
00:02:06.680 --> 00:02:08.654 Therefore, this program will focus on
NOTE Confidence: 0.8278826
00:02:08.654 --> 00:02:10.955 work being done by our trainees and
NOTE Confidence: 0.8278826
00:02:10.955 --> 00:02:13.097 not really on my own personal work.
NOTE Confidence: 0.8278826
00:02:13.100 --> 00:02:15.459 I will just be introducing the topics.
NOTE Confidence: 0.8278826
00:02:15.460 --> 00:02:18.316 And our vision and goals for the
NOTE Confidence: 0.8278826
00:02:18.316 --> 00:02:20.119 Interventional Oncology Program at Yale.
NOTE Confidence: 0.8278826
00:02:20.120 --> 00:02:22.829 So this session, as you may recall,
NOTE Confidence: 0.8278826
00:02:22.830 --> 00:02:25.014 was originally planned for March 10th
NOTE Confidence: 0.8278826
00:02:25.014 --> 00:02:28.258 and it was just after the kovid pandemic.
NOTE Confidence: 0.8278826
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 am 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

NOTE Confidence: 0.8278826
00:03:04.374 --> 00:03:06.834 then will be followed by Jessica

NOTE Confidence: 0.8278826
00:03:06.834 --> 00:03:09.398 Santana and tells Evie who are both

NOTE Confidence: 0.8278826
00:03:09.398 --> 00:03:11.559 graduate students in our lab and

NOTE Confidence: 0.8278826
00:03:11.559 --> 00:03:13.869 the work will all be talking about

NOTE Confidence: 0.8278826
00:03:13.869 --> 00:03:16.129 liver cancer and Interventional

NOTE Confidence: 0.8278826
00:03:16.129 --> 00:03:17.986 oncology related activities.

NOTE Confidence: 0.8278826
00:03:17.990 --> 00:03:20.874 So let me just share my screen.

NOTE Confidence: 0.9124253
00:03:27.170 --> 00:03:30.610 OK, so. Really,

NOTE Confidence: 0.9124253
00:03:30.610 --> 00:03:32.250 what is Interventional oncology?

NOTE Confidence: 0.9124253
00:03:32.250 --> 00:03:34.395 Well intermixed oncology is a

NOTE Confidence: 0.9124253
00:03:34.395 --> 00:03:35.682 subspecialty of Interventional

NOTE Confidence: 0.9124253
00:03:35.682 --> 00:03:37.419 radiology that utilizes minimally

NOTE Confidence: 0.9124253
00:03:37.419 --> 00:03:39.063 invasive image guided procedures

NOTE Confidence: 0.9124253
00:03:39.063 --> 00:03:41.491 to both diagnosis and treat patients

NOTE Confidence: 0.9124253
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 as well as having minimal systemic side effects leading to an overall improved. and time Efficacy, as well as having minimal systemic side effects leading to an overall improved. Quality of life.

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 you know 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,
translational and clinical research.

We do have some work to do in this regard,

but I must say I was really thrilled to see when I was in 2016 as an invited faculty of Asco GI.

My discipline next to my name was listed actually as an Interventional Oncologist,

not an interventional radiologist,

so I was really happy at that time,

and I thought we actually made it.

However,

I really do believe that in terms of research and education of referring physicians,

I think we’re nearly there and on the right track,

but I don’t know if we’ve come there totally.
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 proximity to the heart. Fortunately we were able to get adequate tissue sampling and help this patient get the appropriate chemotherapy 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
NOTE Confidence: 0.7713822
required to bulking are typically
NOTE Confidence: 0.7713822
done in an outpatient setting setting
NOTE Confidence: 0.7713822
and these procedures are repeatable.
NOTE Confidence: 0.7713822
So if we can see here we have
NOTE Confidence: 0.7713822
radiofrequency ablation and microwave
NOTE Confidence: 0.7713822
which are heat based therapies.
NOTE Confidence: 0.7713822
We have Cryo Ablation which is a coal
NOTE Confidence: 0.7713822
based therapy and we actually have
NOTE Confidence: 0.7713822
irreversible electroporation which
NOTE Confidence: 0.7713822
is really to electrocute the tumors.
NOTE Confidence: 0.7713822
Believe it or not,
NOTE Confidence: 0.7713822
by changing the ionic potentials
NOTE Confidence: 0.7713822
between the membranes.
NOTE Confidence: 0.7713822
So ablation of liver tumors,
NOTE Confidence: 0.7713822
which is in this was its initial indication,
as shown here in. 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? Follow up. This is a patient who,
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

So she had actually no.

So we used Ayari again, that’s basically electrocution, which is technically a non thermal ablation.

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.

He We see a case of a patient with HIV, cirrhosis and a 4.8 centimeters segment. 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 count of 57 who also needs treatment.
There’s a bridge to transplant.
This tumor is shown here is in a very difficult location,
and she successfully underwent embolization with no residual tumor,
and this patient also underwent liver transplantation.
Here we’re able to see a patient that was treated in their 90s who has a large HTC.
In this case, the ACC actually ruptured through the capsule,
and as you probably are all aware,
this is associated with poor, if not dismal, 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 an 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 IO
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
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 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 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,
this is very transitional area where both
seemed to be interacting quite extensively.
We saw a lot of clinical trials focusing an overlap of those therapies, and this is exactly the realm where most patients are being diagnosed and also the realm where we think there is most room of improvement for patient outcomes, so systemic therapies for HTC then and now I borrowed the slides from Agusan Abou Alfa, who’s? and this is how the market look like. Five years ago we just had one drug 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 glucose metabolism. And so called the Arabic and anaerobic glycolysis, and well,
00:16:20.866 --> 00:16:23.990 the glucose is being taken up with that sell.

00:16:23.990 --> 00:16:25.010 It produces lactate.

00:16:25.010 --> 00:16:26.710 It is that essentially is

00:16:26.710 --> 00:16:28.840 D Cup from the Krebs cycle,

00:16:28.840 --> 00:16:29.779 and this lacked.

00:16:29.779 --> 00:16:31.657 It is then being flooded directly

00:16:31.657 --> 00:16:34.029 into the extra seller micro environment.

00:16:34.030 --> 00:16:35.824 And because of that there was

00:16:35.824 --> 00:16:37.508 dramatic acidification of the

00:16:37.508 --> 00:16:39.220 surrounding tumor micro environment.

00:16:39.220 --> 00:16:41.988 And what does that really mean for us?

00:16:41.990 --> 00:16:44.060 The extracellular pH and liver cancer,

00:16:44.060 --> 00:16:45.444 especially aggressive age species

00:16:45.444 --> 00:16:47.382 known to be very, very low.

00:16:47.382 --> 00:16:50.122 And now finding say that this is a very
important exclusion mechanism for four.

NOTE Confidence: 0.8167382

Immune cells and the mechanism of immune cell exhaustion.

NOTE Confidence: 0.8167382

So this has been previously reported and we now know more than ever that actually tumor infiltrating T lymphocytes depend extremely on extra seller acidity and competitive glucose deprivation,

NOTE Confidence: 0.8167382

and that the reversal of this hostile tumor micro environment can actually improve their infiltration into the tumor.

NOTE Confidence: 0.8167382

An immune response.

NOTE Confidence: 0.8167382

So to sum it up,

NOTE Confidence: 0.8167382

loads for seller pH is a marker of tumor aggressiveness and the presence of Protons and lactate really protects
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? Theoretically this is an embolus therapy that changes the tumor microenvironment. And what happens is that in theory tastes me potentially exacerbate a hostile tumor microenvironment 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 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 is necrotic tumor packed with drug eluting beads. And surrounding that we see a very
00:18:50.507 --> 00:18:51.830 dense immune infiltrate and if
NOTE Confidence: 0.8167382
00:18:51.830 --> 00:18:53.230 we zoom in We really almost see
NOTE Confidence: 0.8167382
00:18:53.230 --> 00:18:54.971 a secondary immune follicles and
NOTE Confidence: 0.8167382
00:18:54.971 --> 00:18:56.826 macrophages and T cells really
NOTE Confidence: 0.8167382
00:18:56.826 --> 00:18:58.160 accumulating the transitional zone.
NOTE Confidence: 0.8167382
00:18:58.160 --> 00:19:01.716 But they can’t really penetrate
NOTE Confidence: 0.8167382
00:19:01.716 --> 00:19:03.599 into the necrotic areas of the tumor
NOTE Confidence: 0.8167382
00:19:03.600 --> 00:19:04.485 Why is that?
NOTE Confidence: 0.8167382
00:19:04.485 --> 00:19:06.550 So our mission was at this point
NOTE Confidence: 0.8167382
00:19:06.617 --> 00:19:08.741 to really look at the underlying
NOTE Confidence: 0.8167382
00:19:08.741 --> 00:19:11.470 mechanisms and how do systemic therapies.
NOTE Confidence: 0.8167382
00:19:11.470 --> 00:19:13.661 How does in the immune system and
NOTE Confidence: 0.8167382
00:19:13.661 --> 00:19:15.140 local regional therapies interact?
NOTE Confidence: 0.8167382
00:19:15.140 --> 00:19:17.186 So we wanted to develop imaging
NOTE Confidence: 0.8167382
00:19:17.186 --> 00:19:18.550 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 because that partnered in design and
work on the 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 the noninvasive measurement affects your seller pH and this is where our msit based spectroscopic
Birds methodology comes into place. This has been established previously in brain tumors by Daniel. And we have translated this essentially to deliver.

This is NMR Spectra, scopic method that measures the redundant deviation of shifts and temperature in the region of the tumor, and we can generate the 3D extracellular pH map that provides us with essentially a very accurate characterization of the tumor micro environment. So if we look at the tumor in by itself and measure it as compared to the surrounding liver tissue,
we see that the tumor in 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...
00:21:57.510 --> 00:21:59.335 treat those tumors and measured the
NOTE Confidence: 0.8162481
00:21:59.335 --> 00:22:01.833 pH and as opposed to most of the
NOTE Confidence: 0.8162481
00:22:01.833 --> 00:22:03.975 assumptions that taste is going to
NOTE Confidence: 0.8162481
00:22:03.975 --> 00:22:06.106 actually exacerbate the The Anti.
NOTE Confidence: 0.8162481
00:22:06.106 --> 00:22:09.262 Yeah, I mean the logic, the immune,
NOTE Confidence: 0.8162481
00:22:09.262 --> 00:22:10.846 evasive tumor micro environment,
NOTE Confidence: 0.8162481
00:22:10.850 --> 00:22:12.830 it actually did the opposite.
NOTE Confidence: 0.8162481
00:22:12.830 --> 00:22:15.028 So what we see is a normalization
NOTE Confidence: 0.8162481
00:22:15.028 --> 00:22:17.608 of the tumor pH towards almost
NOTE Confidence: 0.8162481
00:22:17.608 --> 00:22:19.177 delivered background levels.
NOTE Confidence: 0.8162481
NOTE Confidence: 0.8162481
00:22:20.281 --> 00:22:22.483 And that is an important finding
NOTE Confidence: 0.8162481
00:22:22.483 --> 00:22:24.628 because that gives us an opportunity
NOTE Confidence: 0.8162481
00:22:24.628 --> 00:22:26.877 to use local regional therapy in
NOTE Confidence: 0.8162481
NOTE Confidence: 0.8162481
00:22:28.749 --> 00:22:30.153 checkpoint 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,
butter with taste and bicarb,
especially improving and elevating a pH,
you see massive intratumoral infiltration of immune cells,
and that’s an important finding that we made here in oncology.
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, 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, Montgomery, 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 infiltration.
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 and we 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 Marsh
00:25:33.349 --> 00:25:35.166 higher focal resolution where we
label antibodies with gadolinium
and then inject them

00:25:38.297 --> 00:25:40.613 directly into those tumors and through
the artery, and we can see that there is
very specific accumulation and staining.

00:25:43.896 --> 00:25:50.607 that we can now really localize characterize,
and that’s a big step forward
because not only can we now image the tumor
and functionality of immune cells.

00:25:55.780 --> 00:26:00.694 we can also images from a presence
and 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 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.
today than we have in 2013, and so that is a huge challenge. Anne, it’s David already presented.

We have different flavors of chemo embolization, embolization with drug alluding Beatson Radio mobilization.

We have a variety of different methodologies in ways how we can introduce tumor necrosis, cold heat,

and electrocution in a way we have five different and more coming up with systemic therapy agents, all of which pose different changes.
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
00:28:37.544 --> 00:28:39.100 artificial intelligence now comes in.

NOTE Confidence: 0.86596924

00:28:39.100 --> 00:28:41.038 And this is essentially data driven.

NOTE Confidence: 0.86596924

00:28:41.040 --> 00:28:42.912 Learning that deep down can be

NOTE Confidence: 0.86596924

00:28:42.912 --> 00:28:44.532 explained as machine learning that

NOTE Confidence: 0.86596924

00:28:44.532 --> 00:28:46.434 recognizes trends and objects in pre

NOTE Confidence: 0.86596924

00:28:46.434 --> 00:28:48.169 labeled patterns or deep learning,

NOTE Confidence: 0.86596924

00:28:48.170 --> 00:28:50.403 and tall is going to be talking

NOTE Confidence: 0.86596924

00:28:50.403 --> 00:28:51.840 more about that where?

NOTE Confidence: 0.86596924

00:28:51.840 --> 00:28:53.838 We use those networks to actually

NOTE Confidence: 0.86596924

00:28:53.838 --> 00:28:55.928 learn from data without pre labeling

NOTE Confidence: 0.86596924

00:28:55.928 --> 00:28:58.028 the outcome and that may hopefully

NOTE Confidence: 0.86596924

00:28:58.028 --> 00:28:59.960 increase the workflow efficiency,

NOTE Confidence: 0.86596924

00:28:59.960 --> 00:29:01.695 improve our diagnostic accuracy really

NOTE Confidence: 0.86596924

00:29:01.695 --> 00:29:02.736 enabled predictive recommendations

NOTE Confidence: 0.86596924

00:29:02.736 --> 00:29:04.248 for us Taylor Personalized

NOTE Confidence: 0.86596924
Therapeutic recommendations and help

us 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 Inter procedural 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 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, really appreciate those collaborations that are increasingly interdisciplinary.

Mean radiology have a very large biomedical imaging collaborative network, and I want to thank from Eden, Daniel, and Larry and everyone mentioned here.

I'll say I'll.

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 more students that work with us.

First, 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 focusing on predicting outcome and
recurrence of HTC after intervention.

And I'd like to.

And now the stop sharing the screen and give it to Jessica.

Hi all, I'm Jessica. I am a master level demonologist Anna graduate student at the Yale Interventional College Lab and I'm very excited today to be presenting my work, titled, Noninvasive molecular imaging allows characterization of the immune response following hepatic radiofrequency Ablation in a mouse model. 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

NOTE Confidence: 0.84324324
00:32:45.210 --> 00:32:48.073 An Protogenic Side effects as well as
NOTE Confidence: 0.84324324
00:32:48.073 --> 00:32:51.034 abscopal effects that in turn can positively
NOTE Confidence: 0.84324324
00:32:51.034 --> 00:32:53.530 impact the immune response to cancer.
NOTE Confidence: 0.84324324
00:32:53.530 --> 00:32:54.002 However,
NOTE Confidence: 0.84324324
00:32:54.002 --> 00:32:56.834 we have currently no instruments that
NOTE Confidence: 0.84324324
00:32:56.834 --> 00:32:59.871 would allow us to non invasively
NOTE Confidence: 0.84324324
00:32:59.871 --> 00:33:01.919 monitor such immune response.
NOTE Confidence: 0.84324324
00:33:01.920 --> 00:33:04.280 So the purpose of this work is to
NOTE Confidence: 0.84324324
00:33:04.280 --> 00:33:06.556 develop a noninvasive molecular imaging
NOTE Confidence: 0.84324324
00:33:06.556 --> 00:33:09.236 instruments to visualize such immune
NOTE Confidence: 0.84324324
00:33:09.236 --> 00:33:12.380 response to thermal injury following RFA.
NOTE Confidence: 0.815851800000001
00:33:14.430 --> 00:33:16.880 So our group has built a translation
NOTE Confidence: 0.815851800000001
00:33:16.880 --> 00:33:18.881 of mouse model of radiofrequency
NOTE Confidence: 0.815851800000001
00:33:18.881 --> 00:33:21.954 ablation as a platform to develop and
NOTE Confidence: 0.815851800000001
00:33:21.954 --> 00:33:24.360 validate mirbase dimona probes for in
NOTE Confidence: 0.815851800000001
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 of Iran and 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, right? 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.
We have confirmed that there is a local
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.
00:37:00.760 --> 00:37:02.857 of 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
00:37:07.360 --> 00:37:08.900 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
00:37:14.230 --> 00:37:16.600 And As for our gadolinium based
NOTE Confidence: 0.7773221
00:37:16.600 --> 00:37:21.740 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.
NOTE Confidence: 0.7773221
00:37:38.330 --> 00:37:43.046 So here on your left you have the Ablation.

00:37:43.050 --> 00:37:45.726 Cite the picture taking seconds after ablation showing the ablation site.

00:37:45.726 --> 00:37:51.114 And we also have MRI when we post Ablation After 24 hours with gadolinium city 68 delivered systemically.

00:37:51.114 --> 00:37:55.052 And on your left you have the picture taken, ex Vivo confirming of what we’re seeing on the MRI.

00:37:55.052 --> 00:38:02.092 And to confirm that this parable itional darkroom is seen precisely in animals receiving those city, 68 tagged to 68 antibodies tagged with gadolinium.

00:38:02.100 --> 00:38:04.932 We also ran T1 weighted MRI with gadolinium.

00:38:04.932 --> 00:38:06.820 And on your left you have the picture taken, ex Vivo confirming of what we’re seeing on the MRI.

00:38:06.820 --> 00:38:09.060 And to confirm that this parable itional darkroom is seen precisely in animals receiving those city, 68 tagged to 68 antibodies tagged with gadolinium.

00:38:09.060 --> 00:38:12.124 We also ran T1 weighted MRI with gadolinium.
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

00:38:59.750 -- 00:39:02.030 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
00:39:04.094 --> 00:39:06.382 week post ablation after gadolinium
NOTE Confidence: 0.7773221
00:39:06.382 --> 00:39:08.086 labeled antibody administration,
NOTE Confidence: 0.7773221
00:39:08.090 --> 00:39:10.962 where you can see the rim of the
NOTE Confidence: 0.7773221
00:39:10.962 --> 00:39:12.939 local deposition of the infiltrating
NOTE Confidence: 0.7773221
00:39:12.939 --> 00:39:14.909 cells an on your right.
NOTE Confidence: 0.7773221
00:39:14.910 --> 00:39:17.493 We have the X visual confirmation with
NOTE Confidence: 0.7773221
00:39:17.493 --> 00:39:20.062 the image Ng Masama tree of local
NOTE Confidence: 0.7773221
00:39:20.062 --> 00:39:23.090 deposition of the sea to 68 macrophages.
NOTE Confidence: 0.7773221
00:39:23.090 --> 00:39:25.890 In the transitional zone.
NOTE Confidence: 0.7773221
00:39:25.890 --> 00:39:27.555 So as the main conclusions
NOTE Confidence: 0.7773221
00:39:27.555 --> 00:39:29.220 and findings of this study,
NOTE Confidence: 0.7773221
00:39:29.220 --> 00:39:31.285 it tells us that both spines and
NOTE Confidence: 0.7773221
00:39:31.285 --> 00:39:32.598 Catalina based molecular imaging
NOTE Confidence: 0.7773221
00:39:32.598 --> 00:39:34.074 allows for specific labeling
NOTE Confidence: 0.7773221
00:39:34.074 --> 00:39:35.550 of local immune infiltrate,
and this is also a translation of study with the proof of principle for the visibility of the MRI imaging for macrophages on a 9 point. For Tesla MRI scanners. And also tells us that noninvasive in vivo detection of the immune system can be achieved using dedicated immune probes. An ask for our future perspective and clinical application. We can have this as a useful tool to study and characterize the interplay between the tumor micro environment and the cell opinion selectivity in 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 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 bio medical
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
00:41:33.194 --> 00:41:35.499 could be made by imaging alone,

00:41:35.500 --> 00:41:38.110 sometimes a biopsy may be required

00:41:38.110 --> 00:41:39.850 to support this diagnosis.

00:41:39.850 --> 00:41:44.135 A little bit statistics every 40 seconds at

00:41:44.135 --> 00:41:47.890 patient diagnosed with ATC in 2020 alone,

00:41:47.890 --> 00:41:50.565 the death rate is approximately

00:41:50.565 --> 00:41:52.705 the 800,000 deaths worldwide.

00:41:52.710 --> 00:41:56.448 ATC may recur and there is no

00:41:56.448 --> 00:41:58.796 significant imaging biomarker or

00:41:58.796 --> 00:42:02.056 clinical biomarkers to reliably predict

00:42:02.056 --> 00:42:05.660 recurrence before location to treatment.

00:42:05.660 --> 00:42:08.320 liver transplantation.

00:42:08.320 --> 00:42:10.220 It helps to decrease the

However, we are all aware to the shortness of organs. Therefore, 2 criterias 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...
NOTE Confidence: 0.82661027
00:42:44.614 --> 00:42:48.470 patient to occur within the 1st five years.
NOTE Confidence: 0.82661027
00:42:48.470 --> 00:42:49.970 So as I said,
NOTE Confidence: 0.82661027
00:42:49.970 --> 00:42:51.845 these two criterias location criterias
NOTE Confidence: 0.82661027
00:42:51.845 --> 00:42:54.308 has suffered from false positives,
NOTE Confidence: 0.82661027
00:42:54.310 --> 00:42:55.308 and our hypothesis is that there is more
NOTE Confidence: 0.82661027
00:42:57.198 --> 00:42:59.310 information in radiological images,
NOTE Confidence: 0.82661027
00:42:59.310 --> 00:43:00.978 specifically MRI that correlate
NOTE Confidence: 0.82661027
00:43:00.978 --> 00:43:02.229 with HTC recurrence.
NOTE Confidence: 0.82661027
00:43:02.230 --> 00:43:04.498 Then the naked eye could detect
NOTE Confidence: 0.82661027
00:43:04.498 --> 00:43:07.571 and the way we’re going to try to
NOTE Confidence: 0.82661027
00:43:07.571 --> 00:43:09.791 test this hypothesis is by using
NOTE Confidence: 0.82661027
00:43:09.875 --> 00:43:12.305 deep learning algorithm to extract
NOTE Confidence: 0.82661027
00:43:12.305 --> 00:43:15.804 features from MRI images and try to
NOTE Confidence: 0.82661027
00:43:15.804 --> 00:43:20.060 use them to correlate to ATC re occurrence.
NOTE Confidence: 0.82661027
00:43:20.060 --> 00:43:22.083 And a little bit before I start
NOTE Confidence: 0.82661027
talking about our methodology, I will talk about driven predictive modeling and a little bit of deep learning. So when we talk about driven predictive model, we usually refer to two different variables, which will give up the outcome of our target building which could be recurrent or not. And this predictive models 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.
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 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. Estimate this better. 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 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,
00:46:40.070 --> 00:46:42.030 88 minutes and 32 females.
NOTE Confidence: 0.84268486
00:46:42.030 --> 00:46:44.772 All of them were diagnosed with
NOTE Confidence: 0.84268486
00:46:44.772 --> 00:46:47.839 HTC between there is 2005 to 2018.
NOTE Confidence: 0.84268486
00:46:47.840 --> 00:46:51.564 So the patient went into MRI imaging,
NOTE Confidence: 0.84268486
00:46:51.570 --> 00:46:54.486 then were diagnosed with HTC and
NOTE Confidence: 0.84268486
00:46:54.486 --> 00:46:57.430 then got treatment 29 oblations,
NOTE Confidence: 0.84268486
00:46:57.430 --> 00:47:01.250 32 receptions and 5:59 presentations.
NOTE Confidence: 0.84268486
00:47:01.250 --> 00:47:03.778 An time went by, some of them recur,
NOTE Confidence: 0.84268486
00:47:03.780 --> 00:47:06.812 and some of them stop their follow which
NOTE Confidence: 0.84268486
00:47:06.812 --> 00:47:09.188 we considered to be non recurrences.
NOTE Confidence: 0.84268486
00:47:09.190 --> 00:47:11.094 To this time that I can call time
NOTE Confidence: 0.84268486
00:47:11.094 --> 00:47:12.816 to recurrence and this would be
NOTE Confidence: 0.84268486
00:47:12.816 --> 00:47:13.707 our explained variable,
NOTE Confidence: 0.84268486
00:47:13.710 --> 00:47:15.900 the variable that we’re going
NOTE Confidence: 0.84268486
00:47:15.900 --> 00:47:17.652 to try to predict.
NOTE Confidence: 0.84268486
00:47:17.660 --> 00:47:19.850 With respect to our input data,
we’re going to use conference enhanced multi phase liver magnetic resonance imaging, MRI, 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.
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 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 we were just involved in a study that was recently published in the Journal of thoracic oncology, which was a prospective clinical
trial called solstice that.

Did show benefits of cold,

you know,

for for lung nodules and then I

already as I kind of explained,

it's kind of a niche application.

Mostly used in pancreas,

but it's in an area where it's
difficult to treat.

Areas which have vital structures

in your body,

so that's the I guess summary

of that so thanks.

So let me ask a follow up question 'cause

you great deal of the work is really

advancing understanding the nature of
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 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 the 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 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 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. And I think we do have an
amazing infrastructure with RMR

Research Center here and the Pet

Center on the other hand 2.

To actually do that kind of research.

So let me ask, given what you’re describing in the nature of the immune.

Fear after procedures such as these.

Desert potentially suggests that any efforts right now to combine a checkpoint inhibitor with tastes or other ablation procedure may not be yet optimized.

Turn to really achieve what we hope they would achieve because of the nature of the environment absolutely,
and this is exactly what I showed.

If you remember one of the slides had different embolic agents,

We’re using various embolic 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
translation 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 the major key point

that we need to address and one of

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
understand that our therapies are necessary in our increasingly combined with systemic therapy, we need to investigate that, and I think that we’re going to have major breakthroughs in the next three to five years. Thank you.

Well, I know where at the top of the hour, and I want to thank Jessica and tile and Julius and David for really a remarkably stimulating body of work and Bradley bring to our attention what can be accomplished in Interventional Onkologie. So you know, thank you for this continued education.
00:58:24.972 --> 00:58:26.867 for the great work you’re doing

NOTE Confidence: 0.84226775

00:58:26.867 --> 00:58:28.736 and everyone on line. Thank you.