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 Cancer Center in our University and health care system and you know, really focused on.
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

doctor Madoff is the Co director

of Interventional Oncology of the

Interventional and college research

Interventional and college research

lab vice chair for clinical research,

the section chief for

Interventional radiology.

An Department of radiology

and biomedical imaging,
and David really has throughout his career 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.
00:01:53.741 --> 00:01:55.643 of a session on the multidisciplinary
management of colorectal liver metastases.

00:01:55.643 --> 00:01:57.689 Today’s session, as you stated it will
be focused on Interventional oncology.

00:02:04.262 --> 00:02:06.678 What it is in some of the exciting
research being done in our lab at Yale.

00:02:08.654 --> 00:02:10.955 work being done by our trainees and
not really on my own personal work.

00:02:15.459 I will just be introducing the topics.

00:02:18.316 And our vision and goals for the
Interventional Oncology Program at Yale.

00:02:22.829 So this session, as you may recall,
was originally planned for March 10th
and it was just after the kovid pandemic.
So interesting, Lee, it’s actually given us more time to make our data even more mature. So for the audience for today, 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
NOTE Confidence: 0.8278826
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 diagnose 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 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 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. 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 proximity to the heart. 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 sparing normal surrounding tissues, treat tissues with unfavorable location or pattern of distribution for resection and 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 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,
00:07:31.440 --> 00:07:32.684 as shown here in.

00:07:32.684 --> 00:07:35.514 This is 1 case of a patient with

00:07:35.514 --> 00:07:38.136 HTC that needed ablation as a

00:07:38.136 --> 00:07:40.030 bridge to transplant.

00:07:40.030 --> 00:07:43.294 As we can see, 2 1/2 years later,

00:07:43.300 --> 00:07:46.919 no tumor recurrence or any residual disease.

00:07:46.920 --> 00:07:49.251 Next was the case of an isolated

00:07:49.251 --> 00:07:50.250 colorectal liver metastasis.

00:07:50.250 --> 00:07:52.707 Who here you see a pet positive

00:07:52.707 --> 00:07:54.471 or hypermetabolic lesion in the

00:07:54.471 --> 00:07:56.711 right lobe of the liver who was

00:07:56.711 --> 00:07:58.040 successfully treated with Ablation

00:07:58.040 --> 00:08:00.573 and his team are free at one year?

00:08:00.573 --> 00:08:01.239 Follow up.

00:08:03.420 --> 00:08:05.080 This is a patient who,
00:08:05.080 --> 00:08:07.066 instead of having a liver lesion,
NOTE Confidence: 0.8226105
00:08:07.070 --> 00:08:08.206 has a lung nodule.
NOTE Confidence: 0.8226105
00:08:08.206 --> 00:08:10.378 Here we can see that based on
NOTE Confidence: 0.8226105
00:08:10.378 --> 00:08:12.378 having heat based thermal ablation,
NOTE Confidence: 0.8226105
00:08:12.380 --> 00:08:15.036 the patient did very well at seven months.
NOTE Confidence: 0.8226105
00:08:15.040 --> 00:08:17.343 As you can see, there’s no residual
NOTE Confidence: 0.8226105
00:08:17.343 --> 00:08:20.812 tumor on the image Ng, and there was no
NOTE Confidence: 0.8226105
00:08:20.812 --> 00:08:23.500 local recurrence seen at three years.
NOTE Confidence: 0.8226105
00:08:23.500 --> 00:08:25.708 We can also treat bone metastasis.
NOTE Confidence: 0.8226105
00:08:25.710 --> 00:08:27.756 This is a patient with metastatic
NOTE Confidence: 0.8226105
00:08:27.756 --> 00:08:29.904 breast carcinoma with a focal right
NOTE Confidence: 0.8226105
00:08:29.904 --> 00:08:32.058 femoral and right hip pain limiting
NOTE Confidence: 0.8226105
00:08:32.058 --> 00:08:33.799 mobility for whatever reason,
NOTE Confidence: 0.8226105
00:08:33.800 --> 00:08:35.312 she refused radiation therapy
NOTE Confidence: 0.8226105
00:08:35.312 --> 00:08:37.580 and was treated with heat based
NOTE Confidence: 0.8226105
00:08:37.645 --> 00:08:39.081 thermal ablation and Samantha
00:08:39.081 --> 00:08:41.658 plasty is shown here and she had
NOTE Confidence: 0.8226105
00:08:41.658 --> 00:08:43.423 an immediate improvement in right
NOTE Confidence: 0.8226105
00:08:43.423 --> 00:08:46.680 femoral pain from 8 to 10 out of 10.
NOTE Confidence: 0.80972403
00:08:49.050 --> 00:08:51.514 This is a very interesting use of
NOTE Confidence: 0.80972403
00:08:51.514 --> 00:08:53.310 thermal ablation in this case,
NOTE Confidence: 0.80972403
00:08:53.310 --> 00:08:54.154 with cryoablation.
NOTE Confidence: 0.80972403
00:08:54.154 --> 00:08:56.264 This patient had metastatic Rectal
NOTE Confidence: 0.80972403
00:08:56.264 --> 00:08:58.138 Squamous Cell Carcinoma who had
NOTE Confidence: 0.80972403
00:08:58.138 --> 00:09:00.056 severe intractable 10 out of 10 pain,
NOTE Confidence: 0.80972403
00:09:00.060 --> 00:09:01.835 secondary to inoperable tumor recurrence
NOTE Confidence: 0.80972403
00:09:01.835 --> 00:09:03.960 infringing on the sacral nerve roots.
NOTE Confidence: 0.80972403
00:09:03.960 --> 00:09:05.875 She was successfully treated with
NOTE Confidence: 0.80972403
00:09:05.875 --> 00:09:08.139 partial cryo ablation of the bowel
NOTE Confidence: 0.80972403
00:09:08.139 --> 00:09:10.363 wall and you can see right here the
NOTE Confidence: 0.80972403
00:09:10.363 --> 00:09:12.659 low density ice she had immediate
NOTE Confidence: 0.80972403
or should say complete resolution

So she had actually no.

Team up until a year,

Lastly we were able to treat this liver tumor here.

That was a budding the left hepatic bile duct.

So we used Ayari again, that’s basically electrocution,

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.

He 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 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 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 IO 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 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 a 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 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 acidification 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.

NOTE Confidence: 0.8167382

Immune cells and the mechanism

NOTE Confidence: 0.8167382

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 depend extremely on extra seller acidity

NOTE Confidence: 0.8167382

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

NOTE Confidence: 0.8167382

tumor aggressiveness and the presence

NOTE Confidence: 0.8167382

of Protons and lactate really protects
cancer against an immune response. It promotes new angiogenesis. The lactic acidosis plays in 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 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 with initially discarded because of that.

So, 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 we see in necrotic tumor packed with in this particular case 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 start 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 the 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

reproduction of an HTC tumor environment and the has a high

model that has a faithful reproduction.

And we used to model of a rabbit liver tumor,

which is so far the only moderate size animal

reproduction of an HTC tumor environment and the has a high

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
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
treat those tumors and measured the pH and as opposed to most of the assumptions that taste is going to actually exacerbate 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,
and immediately at least one day after therapy,
you don’t really see a lot of immune invasion,
but with taste and bicarb, essentially 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, 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.
00:25:01.465 --> 00:25:03.445 and immune cell accumulation in
NOTE Confidence: 0.8515036
00:25:03.445 --> 00:25:05.418 the periphery of those tumors.
NOTE Confidence: 0.8515036
00:25:05.418 --> 00:25:06.970 On T2 MRI sequences,
NOTE Confidence: 0.8515036
00:25:06.970 --> 00:25:09.298 and that was proven in histologically
NOTE Confidence: 0.8515036
00:25:09.298 --> 00:25:10.850 with Prussian blue staining,
NOTE Confidence: 0.8515036
00:25:10.850 --> 00:25:12.438 which stands for iron.
NOTE Confidence: 0.8515036
00:25:12.438 --> 00:25:14.820 And we saw that the spines,
NOTE Confidence: 0.8515036
00:25:14.820 --> 00:25:17.055 the iron oxide particles really
NOTE Confidence: 0.8515036
00:25:17.055 --> 00:25:19.290 deposited and CD11B positive macrophages
NOTE Confidence: 0.8515036
00:25:19.360 --> 00:25:21.262 and we confirmed that later with
NOTE Confidence: 0.8515036
00:25:21.262 --> 00:25:23.581 CD 68 staining and the same thing
NOTE Confidence: 0.8515036
00:25:23.581 --> 00:25:25.555 is true for our induction injection
NOTE Confidence: 0.8515036
00:25:25.555 --> 00:25:26.982 of gadolinium labeled antibodies.
NOTE Confidence: 0.8515036
00:25:26.982 --> 00:25:29.166 You probably heard about this from
NOTE Confidence: 0.8515036
00:25:29.166 --> 00:25:31.059 the molecular imaging using pet,
NOTE Confidence: 0.8515036
00:25:31.060 --> 00:25:33.349 but here we have a much Marsh
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 characterize, and 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

NOTE Confidence: 0.81775826

treat HTC will cause a left shift

NOTE Confidence: 0.81775826

of systemic therapy in the BC else,

NOTE Confidence: 0.81775826

and we really must do some heavy lifting.

NOTE Confidence: 0.81775826

It’s up to art actually to put

NOTE Confidence: 0.81775826

to put the collaboration between

NOTE Confidence: 0.81775826

the Interventional in college and

NOTE Confidence: 0.81775826

Immuno Oncology on the right track.

NOTE Confidence: 0.81775826

From a science perspective we must

NOTE Confidence: 0.81775826

also work more on non invasive

NOTE Confidence: 0.81775826

imaging modalities and we did so with

NOTE Confidence: 0.81775826

the extracellular pH that revealed

NOTE Confidence: 0.81775826

that ace actually is an inducer.

NOTE Confidence: 0.81775826

Profound changes to tumor marker

NOTE Confidence: 0.81775826

environment that may help immunotherapy

NOTE Confidence: 0.81775826

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 and intervention alone college. You must be established in combination
00:27:11.848 --> 00:27:12.757 with each other.
NOTE Confidence: 0.81775826
00:27:12.760 --> 00:27:14.664 We have to have a synergy between
NOTE Confidence: 0.81775826
00:27:14.664 --> 00:27:16.547 the two iOS interventional and Immuno
NOTE Confidence: 0.81775826
00:27:16.547 --> 00:27:19.728 Oncology and it’s up to us to work on that.
NOTE Confidence: 0.81775826
00:27:19.730 --> 00:27:21.185 And that generates another bigger
NOTE Confidence: 0.81775826
00:27:21.185 --> 00:27:23.240 problem that we really workup on very
NOTE Confidence: 0.81775826
00:27:23.240 --> 00:27:24.878 closely with Jim Duncan and collaboration
NOTE Confidence: 0.81775826
00:27:24.878 --> 00:27:27.000 with that group and biomedical engineering.
NOTE Confidence: 0.81775826
00:27:27.000 --> 00:27:28.746 And this is the overwhelming growth
NOTE Confidence: 0.81775826
00:27:28.746 --> 00:27:30.900 of data and will be talking about
NOTE Confidence: 0.81775826
00:27:30.900 --> 00:27:32.144 this little bit later.
NOTE Confidence: 0.81775826
00:27:32.150 --> 00:27:34.566 Tall is going to be presenting on that,
NOTE Confidence: 0.81775826
00:27:34.570 --> 00:27:37.066 so we know that the data that we
NOTE Confidence: 0.81775826
00:27:37.066 --> 00:27:38.700 have specifically in imaging and.
NOTE Confidence: 0.81775826
00:27:38.700 --> 00:27:40.584 Cancer in general explode so we
NOTE Confidence: 0.81775826
00:27:40.584 --> 00:27:42.828 have more than 20 times more data
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
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 tall is going to be talking more about that where? We use those networks to actually learn from data without pre labeling the outcome and that may hopefully increase the workflow efficiency, improve our diagnostic accuracy really enabled predictive recommendations for us Taylor Personalized.
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 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. 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

First, Jessica Santana.

She's going to be talking about taking the molecular imaging really to next level in our new animal models, and tall is going to be talking about his role as Biomedical Engineering graduate student within the bio medical imaging Sciences on focusing on predicting outcome and
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.
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 imuna probe also used in this study, 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. 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.
Spions and as a Redpath

NOTE Confidence: 0.77417207

00:37:00.760 --> 00:37:02.857 correlation we confirm the ex vivo
NOTE Confidence: 0.77417207

00:37:02.857 --> 00:37:05.395 specifically position of the spine.
NOTE Confidence: 0.77417207

00:37:05.395 --> 00:37:07.360 At the transitional zone,
NOTE Confidence: 0.77417207

00:37:07.360 --> 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 --> 00:37:19.460 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 MRI when 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 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

00:38:59.750 --> 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
00:39:04.094 --> 00:39:06.382 week post ablation after gadolinium

00:39:06.382 --> 00:39:08.086 labeled antibody administration,

00:39:08.090 --> 00:39:10.962 where you can see the rim of the

00:39:10.962 --> 00:39:12.939 local deposition of the infiltrating

00:39:12.939 --> 00:39:14.909 cells an on your right.

00:39:14.910 --> 00:39:17.493 We have the X visual confirmation with

00:39:17.493 --> 00:39:20.062 the image Ng Masama tree of local

00:39:20.062 --> 00:39:23.090 deposition of the sea to 68 macrophages.

00:39:23.090 --> 00:39:25.890 In the transitional zone.

00:39:25.890 --> 00:39:27.555 So as the main conclusions

00:39:27.555 --> 00:39:31.285 it tells us that both spines and

00:39:31.285 --> 00:39:32.598 Catalina based molecular imaging

00:39:32.598 --> 00:39:34.074 allows for specific labeling

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 of 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
Hello everyone, my name is Charles and I'm a 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 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 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
patient to occur within the 1st five years.

So as I said, these two criterias location criterias has 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 re occurrence. And a little bit before I start
talking about our methodology,

I will talk about data driven predictive modeling and a little bit of deep learning.

So when we talk about data driven predictive model, we usually refer to two different variables, the Explanatory variable and explain part of our target and we want to take these explanatory variables to feed them into predicted model to 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.
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 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 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 repetitive 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,
even incorporating more imaging modalities.

Thank you very much.

So, so that was really great.

Hope you all were able to see what exciting work word.

Does anybody have any questions?

You know, doing in this lab?

And individuals can certainly submit their questions on chat.

but we did receive one which David you took the Liberty of at least answering online.

But let me for the benefit of all.

Let me just toss this out so

Joseph Cam asked, you know, 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.
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 setting that makes it less ideal than four. For the Heat base, now the one positive thing is we
00:52:23.330 --> 00:52:26.669 shown in some of the in one of the
00:52:26.773 --> 00:52:30.221 cases is that you do get the ice
00:52:30.221 --> 00:52:33.335 ball which has low density ice and
00:52:33.335 --> 00:52:35.580 that actually allows the operator
00:52:35.661 --> 00:52:38.115 to really sculpt the margins where
00:52:38.115 --> 00:52:41.099 you want to treat in other organs.
00:52:41.100 --> 00:52:43.848 Systems like the lung and kidney
00:52:43.848 --> 00:52:47.124 is really a dealers choice so that
00:52:47.124 --> 00:52:49.824 there have been papers on both.
00:52:49.830 --> 00:52:52.296 In terms of using cryoablation or
00:52:52.296 --> 00:52:55.006 heat ablation for those that we were
00:52:55.006 --> 00:52:57.323 just involved in a study that was
00:52:57.403 --> 00:52:59.878 recently published in the Journal
00:52:59.878 --> 00:53:01.363 of thoracic oncology,
00:53:01.370 --> 00:53:04.080 which was a prospective clinical
trial called solstice that. Did show benefits of cold, you know, 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.
00:54:21.704 --> 00:54:23.353 I mean, we're right now.
NOTE Confidence: 0.85417795
00:54:23.353 --> 00:54:25.008 Actually submitting one or an
NOTE Confidence: 0.85417795
00:54:25.008 --> 00:54:26.351 application after the other
NOTE Confidence: 0.85417795
00:54:26.351 --> 00:54:27.926 because we want to investigate
NOTE Confidence: 0.85417795
00:54:27.926 --> 00:54:29.600 exactly those points we generated.
NOTE Confidence: 0.85417795
00:54:29.600 --> 00:54:30.431 This preliminary data.
NOTE Confidence: 0.85417795
00:54:30.431 --> 00:54:32.803 Now we want to take it to the
NOTE Confidence: 0.85417795
00:54:32.803 --> 00:54:34.678 clinical perspective and do also
NOTE Confidence: 0.85417795
00:54:34.678 --> 00:54:36.178 trials and immediate future.
NOTE Confidence: 0.85417795
00:54:36.180 --> 00:54:38.732 So I think there is a couple of
NOTE Confidence: 0.85417795
00:54:38.732 --> 00:54:41.109 limitations that we first need to address,
NOTE Confidence: 0.85417795
00:54:41.110 --> 00:54:43.090 and for the pH Image Ng,
NOTE Confidence: 0.85417795
00:54:43.090 --> 00:54:45.058 this is certainly the contrast agent,
NOTE Confidence: 0.85417795
00:54:45.060 --> 00:54:46.950 which is not done yet.
NOTE Confidence: 0.85417795
00:54:46.950 --> 00:54:48.816 Applied and in the human scenario,
NOTE Confidence: 0.85417795
00:54:48.820 --> 00:54:51.052 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 you, As for the 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.
And so let me as a follow up.
So let me ask, given what you’re
describing in the nature of the immune.
Response, immune environment,
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,

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
00:57:22.461 --> 00:57:24.000 translation that we hope for.
NOTE Confidence: 0.83878195
00:57:24.000 --> 00:57:26.536 Just because we don’t know what we’re doing.
NOTE Confidence: 0.83878195
00:57:26.540 --> 00:57:28.358 Essentially so when we combine Interventional
NOTE Confidence: 0.83878195
00:57:28.358 --> 00:57:30.030 in college and Immuno Oncology,
NOTE Confidence: 0.83878195
00:57:30.030 --> 00:57:32.649 we just go about it and say one size
NOTE Confidence: 0.83878195
00:57:32.649 --> 00:57:35.244 fits all and that is something that I
NOTE Confidence: 0.83878195
00:57:35.244 --> 00:57:37.905 feel like is is the major key point
NOTE Confidence: 0.83878195
00:57:37.905 --> 00:57:40.485 that we need to address and one of
NOTE Confidence: 0.83878195
00:57:40.485 --> 00:57:42.375 these issues is that in Interventional
NOTE Confidence: 0.83878195
00:57:42.375 --> 00:57:44.347 Ecology Community would just did not
NOTE Confidence: 0.83878195
00:57:44.347 --> 00:57:46.313 have the academic culture and you
NOTE Confidence: 0.83878195
00:57:46.313 --> 00:57:48.137 know research environment so far and
NOTE Confidence: 0.83878195
00:57:48.137 --> 00:57:49.760 this is across multiple institutions
NOTE Confidence: 0.83878195
00:57:49.760 --> 00:57:51.180 across our entire community.
NOTE Confidence: 0.83878195
00:57:51.180 --> 00:57:52.830 To actually tackle those topics,
NOTE Confidence: 0.83878195
00:57:52.830 --> 00:57:54.822 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,

00:57:56.544 --> 00:57:58.096 we need to investigate that,

00:57:58.096 --> 00:58:01.410 and I think that we’re going to have major breakthroughs in the next three to five years. Thank you.

00:58:01.410 --> 00:58:03.818 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.