WEBVTT

NOTE duration: ”00:16:53.077”

NOTE Confidence: 0.9641126

00:00:00.160 --> 00:00:01.680 Alright. And then last but

NOTE Confidence: 0.9641126

00:00:01.680 --> 00:00:02.800 not least, we're gonna move

NOTE Confidence: 0.9641126

00:00:02.800 --> 00:00:03.620 to the heart.

NOTE Confidence: 0.9423791

00:00:05.120 --> 00:00:06.879 Is Al here? Yes. Doctor

NOTE Confidence: 0.9423791

00:00:06.879 --> 00:00:08.820 Al Senussis graduated from RPI

NOTE Confidence: 0.9443525

00:00:09.200 --> 00:00:10.559 and earned his medical degree

NOTE Confidence: 0.9443525

00:00:10.559 --> 00:00:12.480 from Vermont, completed residency at

NOTE Confidence: 0.9443525

00:00:12.480 --> 00:00:13.460 University of Oklahoma,

NOTE Confidence: 0.92927873

00:00:13.840 --> 00:00:15.460 cardiac fellowship at Virginia,

NOTE Confidence: 0.90536803

00:00:16.055 --> 00:00:17.114 then around the country.

NOTE Confidence: 0.8656485

00:00:17.415 --> 00:00:19.415 Joined Yale, since nineteen ninety.

NOTE Confidence: 0.8656485

00:00:19.415 --> 00:00:20.454 Served as a director of

NOTE Confidence: 0.8656485

00:00:20.454 --> 00:00:20.954 Weitrick.

NOTE Confidence: 0.89888525

00:00:21.335 --> 00:00:23.195 He's also he also run

NOTE Confidence: 0.89888525

00:00:23.335 --> 00:00:24.395 the radiation safety,

NOTE Confidence: 0.9728242

00:00:24.935 --> 00:00:25.675 the IRB,

NOTE Confidence: 0.946096

00:00:26.055 --> 00:00:28.615 the human safety. And, he's

NOTE Confidence: 0.946096

00:00:28.615 --> 00:00:30.375 a true consummate radiologist and

NOTE Confidence: 0.946096

00:00:30.375 --> 00:00:30.875 cardiologist.

NOTE Confidence: 0.9762265

00:00:31.370 --> 00:00:33.290 Underpaid radiologist, I guess. So

NOTE Confidence: 0.9762265

00:00:33.290 --> 00:00:34.590 let's talk about the heart.

NOTE Confidence: 0.9762265

00:00:34.810 --> 00:00:35.950 Alright. Thank you.

NOTE Confidence: 0.9815913

00:00:41.130 --> 00:00:43.290 So these are current, grant

NOTE Confidence: 0.9815913

00:00:43.290 --> 00:00:45.530 funding and also relationships with

NOTE Confidence: 0.9815913

00:00:45.530 --> 00:00:46.030 industry.

NOTE Confidence: 0.9251455

00:00:47.354 --> 00:00:49.115 So, in two thousand and

NOTE Confidence: 0.9251455

00:00:49.115 --> 00:00:50.715 ten, we established the Yale

NOTE Confidence: 0.9251455

00:00:50.715 --> 00:00:52.635 Translational Research Imaging Center and

NOTE Confidence: 0.9251455

00:00:52.635 --> 00:00:53.995 we have a unique set

NOTE Confidence: 0.9251455

00:00:53.995 --> 00:00:56.475 of, imaging systems. One, a

NOTE Confidence: 0.9251455

00:00:56.475 --> 00:00:58.475 solid state CZT spec sixty

NOTE Confidence: 0.9251455

00:00:58.475 --> 00:01:00.235 four slice CT scanner for

NOTE Confidence: 0.9251455

00:01:00.235 --> 00:01:01.775 focused and whole body imaging.

NOTE Confidence: 0.9609813

00:01:02.180 --> 00:01:03.460 We also have a digital

NOTE Confidence: 0.9609813

00:01:03.460 --> 00:01:04.280 cath lab,

NOTE Confidence: 0.9969504

00:01:04.580 --> 00:01:06.259 and we have now a

NOTE Confidence: 0.9969504

00:01:06.259 --> 00:01:08.659 prototype lower extremity scanner that

NOTE Confidence: 0.9969504

00:01:08.659 --> 00:01:09.479 was built,

NOTE Confidence: 0.9908672

00:01:10.259 --> 00:01:10.580 with,

NOTE Confidence: 0.87417275

00:01:11.060 --> 00:01:12.100 an an r o one

NOTE Confidence: 0.87417275

00:01:12.100 --> 00:01:13.459 grant in collaboration with the

NOTE Confidence: 0.87417275

00:01:13.459 --> 00:01:14.979 engineers at the University of

NOTE Confidence: 0.87417275

00:01:14.979 --> 00:01:15.479 Illinois.

NOTE Confidence: 0.98493433

00:01:15.845 --> 00:01:16.965 And shown here is the

NOTE Confidence: 0.98493433

00:01:16.965 --> 00:01:18.885 system uncovered and covered, and

NOTE Confidence: 0.98493433

00:01:18.885 --> 00:01:20.325 this sits over the table

NOTE Confidence: 0.98493433

00:01:20.325 --> 00:01:21.765 of a conventional scanner to

NOTE Confidence: 0.98493433

00:01:21.765 --> 00:01:23.465 do cardiac and leg imaging.

NOTE Confidence: 0.9702365

00:01:23.765 --> 00:01:24.985 We also have,

NOTE Confidence: 0.9582974

00:01:25.765 --> 00:01:26.725 a state of the art

NOTE Confidence: 0.9582974

00:01:26.725 --> 00:01:28.645 ultrasound system integrated with our

NOTE Confidence: 0.9582974

00:01:28.645 --> 00:01:29.604 cath lab as well as

NOTE Confidence: 0.9582974

00:01:29.604 --> 00:01:31.620 rodent ultrasound and micro spec

NOTE Confidence: 0.9294374

00:01:32.740 --> 00:01:33.860 scanning. So in my lab,

NOTE Confidence: 0.9294374

00:01:33.860 --> 00:01:35.720 we're focused on three principal

NOTE Confidence: 0.9294374

00:01:35.780 --> 00:01:38.180 areas of invest investigation, post

NOTE Confidence: 0.9294374

00:01:38.180 --> 00:01:38.680 myocardial

NOTE Confidence: 0.99922055

00:01:38.980 --> 00:01:39.480 remodeling,

NOTE Confidence: 0.9847964

00:01:40.020 --> 00:01:41.860 lung injury and fibrosis, and

NOTE Confidence: 0.9847964

00:01:41.860 --> 00:01:44.180 peripheral vascular disease. And we've

NOTE Confidence: 0.9847964

00:01:44.180 --> 00:01:45.780 been evaluating a number of

NOTE Confidence: 0.9847964

00:01:45.780 --> 00:01:46.920 molecular targeted,

NOTE Confidence: 0.9525628

00:01:48.485 --> 00:01:49.705 sort of, molecular

NOTE Confidence: 0.93211293

00:01:50.245 --> 00:01:52.165 targets including alterations in the

NOTE Confidence: 0.93211293

00:01:52.165 --> 00:01:54.565 extracellular matrix, in particular matrix

NOTE Confidence: 0.93211293

00:01:54.565 --> 00:01:55.065 metalloproteinases,

NOTE Confidence: 0.9982202

00:01:56.325 --> 00:01:57.465 evaluating angiogenesis,

NOTE Confidence: 0.97610587

00:01:58.165 --> 00:01:59.465 evaluating fibrosis,

NOTE Confidence: 0.9930772

00:02:00.440 --> 00:02:01.100 and fibroblast

NOTE Confidence: 0.97824615

00:02:01.480 --> 00:02:03.820 activation, looking at reactive oxygen

NOTE Confidence: 0.97824615

00:02:03.880 --> 00:02:05.340 species, and more recently,

NOTE Confidence: 0.9874396

00:02:06.120 --> 00:02:08.540 mitochondrial membrane potential in collaboration

NOTE Confidence: 0.9874396

00:02:08.680 --> 00:02:10.440 with George's group. And so

NOTE Confidence: 0.9874396

00:02:10.440 --> 00:02:11.400 we have a number of,

NOTE Confidence: 0.9874396

00:02:11.720 --> 00:02:13.320 SPECT and PET agents that

NOTE Confidence: 0.9874396

00:02:13.320 --> 00:02:15.100 we're evaluating in these conditions.

NOTE Confidence: 0.91643095

00:02:15.955 --> 00:02:17.235 I wanted to highlight some

NOTE Confidence: 0.91643095

00:02:17.235 --> 00:02:18.435 of the other work from,

NOTE Confidence: 0.91643095

00:02:18.834 --> 00:02:21.075 Mehron Sadeghi in cardiology. He

NOTE Confidence: 0.91643095

00:02:21.075 --> 00:02:21.575 also

NOTE Confidence: 0.9719551

00:02:21.955 --> 00:02:23.255 is sort of a cardiac

NOTE Confidence: 0.9719551

00:02:23.315 --> 00:02:25.255 molecular imager, and his lab,

NOTE Confidence: 0.98814774

00:02:25.875 --> 00:02:26.375 focuses,

NOTE Confidence: 0.75871503

00:02:27.075 --> 00:02:27.575 again,

NOTE Confidence: 0.90851474

00:02:28.080 --> 00:02:28.400 on,

NOTE Confidence: 0.9850552

00:02:29.040 --> 00:02:30.660 activation of matrix metalloproteinases

NOTE Confidence: 0.97818077

00:02:31.280 --> 00:02:32.959 and tissue remodeling more in

NOTE Confidence: 0.97818077

00:02:32.959 --> 00:02:34.319 the vascular space than the

NOTE Confidence: 0.97818077

00:02:34.319 --> 00:02:36.319 cardiac space. He also is

NOTE Confidence: 0.97818077

00:02:36.319 --> 00:02:38.639 developing some collagen based imaging

NOTE Confidence: 0.97818077

00:02:38.639 --> 00:02:40.019 agents to look at fibrosis

NOTE Confidence: 0.89926255

00:02:40.835 --> 00:02:42.455 and and a more targeted,

NOTE Confidence: 0.9480474

00:02:43.155 --> 00:02:44.535 agent to look at MMP

NOTE Confidence: 0.9480474

00:02:44.595 --> 00:02:45.095 twelve.

NOTE Confidence: 0.985792

00:02:45.395 --> 00:02:47.075 And this involves looking at

NOTE Confidence: 0.985792

00:02:47.075 --> 00:02:49.875 aortic aneurysms, pulmonary fibrosis, and

NOTE Confidence: 0.985792

00:02:49.875 --> 00:02:50.375 granulomatous

NOTE Confidence: 0.96873194

00:02:50.755 --> 00:02:52.435 lung disease. And he's been

NOTE Confidence: 0.96873194

00:02:52.435 --> 00:02:52.935 working

NOTE Confidence: 0.891402

00:02:53.315 --> 00:02:54.595 at both SPECT and PET

NOTE Confidence: 0.891402

00:02:54.595 --> 00:02:56.135 agents and has one,

NOTE Confidence: 0.972939

00:02:57.050 --> 00:02:58.250 sort of agent that they're

NOTE Confidence: 0.972939

00:02:58.250 --> 00:02:59.370 moving to first in man

NOTE Confidence: 0.972939

00:02:59.370 --> 00:03:00.030 in collaboration

NOTE Confidence: 0.890213

00:03:00.330 --> 00:03:01.150 with WashU.

NOTE Confidence: 0.988678

00:03:03.770 --> 00:03:04.889 And then also just to

NOTE Confidence: 0.988678

00:03:04.889 --> 00:03:06.169 highlight some of the work

NOTE Confidence: 0.988678

00:03:06.169 --> 00:03:07.370 that George has been doing

NOTE Confidence: 0.988678

00:03:07.370 --> 00:03:08.110 in the cardiovascular

NOTE Confidence: 0.9704358

00:03:08.570 --> 00:03:10.090 space. So he's developed a

NOTE Confidence: 0.9704358

00:03:10.090 --> 00:03:10.590 novel,

NOTE Confidence: 0.8969433

00:03:11.130 --> 00:03:12.975 radio labeled pet agent that

NOTE Confidence: 0.8969433

00:03:12.975 --> 00:03:15.155 looks at mitochondrial membrane potential.

NOTE Confidence: 0.96259755

00:03:15.694 --> 00:03:17.135 And he's sort of developed

NOTE Confidence: 0.96259755

00:03:17.135 --> 00:03:19.375 the quantitative tools associated with

NOTE Confidence: 0.96259755

00:03:19.375 --> 00:03:20.834 this agent, developing,

NOTE Confidence: 0.98142606

00:03:21.535 --> 00:03:24.014 complex kinetic modeling, optimizing the

NOTE Confidence: 0.98142606

00:03:24.014 --> 00:03:24.514 acquisitions,

NOTE Confidence: 0.8991379

00:03:25.294 --> 00:03:26.735 evaluating the use of this

NOTE Confidence: 0.8991379

00:03:26.735 --> 00:03:29.130 agent in models like chemotherapy

NOTE Confidence: 0.8991379

00:03:29.270 --> 00:03:30.169 induced cardiotoxicity,

NOTE Confidence: 0.95158815

00:03:30.710 --> 00:03:31.830 and has moved it into

NOTE Confidence: 0.95158815

00:03:31.830 --> 00:03:33.430 first in man, and has

NOTE Confidence: 0.95158815

00:03:33.430 --> 00:03:35.270 now has an active IND

NOTE Confidence: 0.95158815

00:03:35.270 --> 00:03:36.390 in this space. And we've

NOTE Confidence: 0.95158815

00:03:36.390 --> 00:03:37.830 been helping him do some

NOTE Confidence: 0.95158815

00:03:37.830 --> 00:03:39.190 of the preclinical work to

NOTE Confidence: 0.95158815

00:03:39.190 --> 00:03:40.310 finish up the work that

NOTE Confidence: 0.95158815

00:03:40.310 --> 00:03:42.090 he initiated at MGH.

NOTE Confidence: 0.9487314

00:03:43.975 --> 00:03:45.175 So I wanted to kinda

NOTE Confidence: 0.9487314

00:03:45.175 --> 00:03:47.035 talk primarily about our work,

NOTE Confidence: 0.9806299

00:03:47.335 --> 00:03:48.235 in theranostics

NOTE Confidence: 0.9154764

00:03:48.535 --> 00:03:49.355 in the cardiovascular

NOTE Confidence: 0.9261112

00:03:49.655 --> 00:03:50.715 space, and this

NOTE Confidence: 0.9981045

00:03:51.015 --> 00:03:52.055 is based on the use

NOTE Confidence: 0.9981045

00:03:52.055 --> 00:03:52.715 of theranostic

NOTE Confidence: 0.887761

00:03:53.015 --> 00:03:53.515 hydrogels.

NOTE Confidence: 0.99602187

00:03:54.055 --> 00:03:55.335 Talk about how we deliver

NOTE Confidence: 0.99602187

00:03:55.335 --> 00:03:57.115 these hydrogels to the heart,

NOTE Confidence: 0.9811402

00:03:57.510 --> 00:03:59.450 how these hydrogels can modulate

NOTE Confidence: 0.9811402

00:03:59.510 --> 00:04:01.050 post infarct remodeling,

NOTE Confidence: 0.9746765

00:04:01.990 --> 00:04:03.270 and how they're a vehicle

NOTE Confidence: 0.9746765

00:04:03.270 --> 00:04:04.010 for delivering,

NOTE Confidence: 0.9829189

00:04:04.470 --> 00:04:06.390 therapies. Well, we're also applying

NOTE Confidence: 0.9829189

00:04:06.390 --> 00:04:07.750 some of these in lung

NOTE Confidence: 0.9829189

00:04:07.750 --> 00:04:08.650 injury models,

NOTE Confidence: 0.91814995

00:04:09.350 --> 00:04:10.250 and developing,

NOTE Confidence: 0.9874442

00:04:11.030 --> 00:04:11.530 percutaneous

NOTE Confidence: 0.8937624

00:04:11.910 --> 00:04:13.985 non invasive approaches to deliver

NOTE Confidence: 0.8937624

00:04:14.125 --> 00:04:15.584 these theranostic hydrogels.

NOTE Confidence: 0.998463

00:04:16.445 --> 00:04:18.044 So these hydrogels can be

NOTE Confidence: 0.998463

00:04:18.044 --> 00:04:18.544 engineered

NOTE Confidence: 0.8623636

00:04:19.005 --> 00:04:20.544 to adjust a biocompatibility,

NOTE Confidence: 0.99730515

00:04:21.404 --> 00:04:23.345 degradation, mechanical properties,

NOTE Confidence: 0.9687552

00:04:23.805 --> 00:04:25.805 their conductivity, as well as

NOTE Confidence: 0.9687552

00:04:25.805 --> 00:04:27.005 our focus has been on

NOTE Confidence: 0.9687552

00:04:27.005 --> 00:04:28.225 making them imageable

NOTE Confidence: 0.98559403

00:04:28.580 --> 00:04:30.180 so that we can, highlight

NOTE Confidence: 0.98559403

00:04:30.180 --> 00:04:31.160 where they're delivered.

NOTE Confidence: 0.99133253

00:04:31.860 --> 00:04:33.480 They've been used to address

NOTE Confidence: 0.99133253

00:04:33.540 --> 00:04:35.800 a number of targeted molecular

NOTE Confidence: 0.99133253

00:04:35.860 --> 00:04:37.380 processes, and they do offer

NOTE Confidence: 0.99133253

00:04:37.380 --> 00:04:39.320 some basic mechanical support.

NOTE Confidence: 0.9970398

00:04:39.860 --> 00:04:41.380 When we deliver these agents,

NOTE Confidence: 0.9970398

00:04:41.380 --> 00:04:42.580 they can be delivered either

NOTE Confidence: 0.9970398

00:04:42.580 --> 00:04:43.480 by a catheter,

NOTE Confidence: 0.9694557

00:04:44.295 --> 00:04:45.975 into the endocardial of the

NOTE Confidence: 0.9694557

00:04:45.975 --> 00:04:46.935 heart or they can be

NOTE Confidence: 0.9694557

00:04:46.935 --> 00:04:47.435 delivered

NOTE Confidence: 0.9642924

00:04:47.735 --> 00:04:48.235 pericardially

NOTE Confidence: 0.99123555

00:04:48.615 --> 00:04:49.515 or epicardially

NOTE Confidence: 0.9677441

00:04:50.135 --> 00:04:51.355 or they can be delivered

NOTE Confidence: 0.9677441

00:04:51.415 --> 00:04:53.035 into the coronary arteries.

NOTE Confidence: 0.9374341

00:04:53.815 --> 00:04:55.255 We've been focused on the

NOTE Confidence: 0.9374341

00:04:55.255 --> 00:04:57.195 local delivery of in inhibitors

NOTE Confidence: 0.9374341

00:04:57.495 --> 00:04:58.555 of matrix metalloproteinases.

NOTE Confidence: 0.97972816

00:05:00.289 --> 00:05:02.210 So again, when we we

NOTE Confidence: 0.97972816

00:05:02.529 --> 00:05:04.789 there were shear thinning, hydrogels

NOTE Confidence: 0.97972816

00:05:04.930 --> 00:05:05.810 that were developed by the

NOTE Confidence: 0.97972816

00:05:05.810 --> 00:05:06.930 group at UPenn, and we

NOTE Confidence: 0.97972816

00:05:06.930 --> 00:05:08.310 wanted to make those imageable.

NOTE Confidence: 0.97972816

00:05:08.370 --> 00:05:09.089 And we had to make

NOTE Confidence: 0.97972816

00:05:09.089 --> 00:05:10.529 sure that when we added

NOTE Confidence: 0.97972816

00:05:10.529 --> 00:05:11.029 iodinated

NOTE Confidence: 0.99678147

00:05:11.410 --> 00:05:13.285 agents to these polymers, it

NOTE Confidence: 0.99678147

00:05:13.285 --> 00:05:15.205 didn't change the mechanical properties

NOTE Confidence: 0.99678147

00:05:15.205 --> 00:05:16.185 of those agents.

NOTE Confidence: 0.874178

00:05:16.725 --> 00:05:18.885 And so, initial studies were

NOTE Confidence: 0.874178

00:05:18.885 --> 00:05:20.645 done in acute, in an

NOTE Confidence: 0.874178

00:05:20.645 --> 00:05:21.145 acute

NOTE Confidence: 0.9182034

00:05:21.525 --> 00:05:23.545 setting of infarction, uninfarcted

NOTE Confidence: 0.7862499

00:05:23.925 --> 00:05:24.425 animals,

NOTE Confidence: 0.97957504

00:05:24.805 --> 00:05:27.060 delivering them surgically with a,

NOTE Confidence: 0.97957504

00:05:27.139 --> 00:05:28.419 kind of a guiding grid

NOTE Confidence: 0.97957504

00:05:28.419 --> 00:05:29.460 that it would assure us

NOTE Confidence: 0.97957504

00:05:29.460 --> 00:05:30.740 that we could deliver these

NOTE Confidence: 0.97957504

00:05:30.740 --> 00:05:31.240 intramyocardial.

NOTE Confidence: 0.9769667

00:05:32.180 --> 00:05:33.220 And so you can see

NOTE Confidence: 0.9769667

00:05:33.220 --> 00:05:33.720 here,

NOTE Confidence: 0.96202964

00:05:34.260 --> 00:05:34.900 I don't know if you

NOTE Confidence: 0.96202964

00:05:34.900 --> 00:05:36.260 can see my pointer here,

NOTE Confidence: 0.96202964

00:05:36.260 --> 00:05:37.800 you can see these iodinated

NOTE Confidence: 0.96202964

00:05:37.940 --> 00:05:39.779 hydrogels that we've delivered in

NOTE Confidence: 0.96202964

00:05:39.779 --> 00:05:40.839 the middle of the myocardium

NOTE Confidence: 0.96202964

00:05:41.060 --> 00:05:42.635 and in three d imaging,

NOTE Confidence: 0.96202964

00:05:42.635 --> 00:05:44.175 we can see them distributed

NOTE Confidence: 0.96202964

00:05:44.235 --> 00:05:45.115 and we can see them

NOTE Confidence: 0.96202964

00:05:45.115 --> 00:05:46.575 within the infarct area.

NOTE Confidence: 0.9754499

00:05:47.595 --> 00:05:48.955 So now we've been for

NOTE Confidence: 0.9754499

00:05:48.955 --> 00:05:50.255 many years evaluating,

NOTE Confidence: 0.98091084

00:05:50.875 --> 00:05:52.795 agents that, look at matrix

NOTE Confidence: 0.98091084

00:05:52.795 --> 00:05:53.295 metalloproteinase.

NOTE Confidence: 0.97820395

00:05:53.755 --> 00:05:54.735 These are macrocyclic

NOTE Confidence: 0.777834

00:05:55.035 --> 00:05:56.395 pepto mimetics that are radio

NOTE Confidence: 0.777834

00:05:56.395 --> 00:05:57.360 labeled that bind to the

NOTE Confidence: 0.777834

00:05:57.360 --> 00:05:58.900 catalytic site of MMPs

NOTE Confidence: 0.9423233

00:05:59.279 --> 00:06:01.219 and look at in vivo

NOTE Confidence: 0.9423233

00:06:01.360 --> 00:06:02.659 balance of temp,

NOTE Confidence: 0.73649347

00:06:03.279 --> 00:06:04.099 m MMP

NOTE Confidence: 0.95268846

00:06:04.719 --> 00:06:06.240 sort of balance. And they're

NOTE Confidence: 0.95268846

00:06:06.240 --> 00:06:06.740 nonspecific

NOTE Confidence: 0.9576829

00:06:07.199 --> 00:06:08.639 and they target a host

NOTE Confidence: 0.9576829

00:06:08.639 --> 00:06:10.080 of MMPs that are known

NOTE Confidence: 0.9576829

00:06:10.080 --> 00:06:11.199 to be involved in post

NOTE Confidence: 0.9576829

00:06:11.199 --> 00:06:12.180 infarctal modeling.

NOTE Confidence: 0.99538577

00:06:12.495 --> 00:06:14.195 We have an STTR grant

NOTE Confidence: 0.97916985

00:06:14.574 --> 00:06:15.154 to develop,

NOTE Confidence: 0.9767216

00:06:16.335 --> 00:06:18.654 GMP grade compound, and and

NOTE Confidence: 0.9767216

00:06:18.654 --> 00:06:20.095 now we've done the final

NOTE Confidence: 0.9767216

00:06:20.095 --> 00:06:21.695 validation runs, and we're hoping

NOTE Confidence: 0.9767216

00:06:21.695 --> 00:06:23.154 to submit the final documents

NOTE Confidence: 0.9767216

00:06:23.214 --> 00:06:24.654 to the FDA for first

NOTE Confidence: 0.9767216

00:06:24.654 --> 00:06:25.714 in human studies.

NOTE Confidence: 0.96097225

00:06:27.000 --> 00:06:28.279 So the the early work

NOTE Confidence: 0.96097225

00:06:28.279 --> 00:06:30.300 we did was in collaboration

NOTE Confidence: 0.96097225

00:06:30.360 --> 00:06:31.160 with the group in the

NOTE Confidence: 0.96097225

00:06:31.160 --> 00:06:32.760 University of South Carolina where

NOTE Confidence: 0.96097225

00:06:32.760 --> 00:06:34.380 we were delivering bioresponsive

NOTE Confidence: 0.95938987

00:06:34.920 --> 00:06:36.760 hydrogels. These are hydrogels that

NOTE Confidence: 0.95938987

00:06:36.760 --> 00:06:37.960 break down in the presence

NOTE Confidence: 0.95938987

00:06:37.960 --> 00:06:38.620 of MMPs

NOTE Confidence: 0.8825603

00:06:39.000 --> 00:06:41.320 and locally release recombinant TINP

NOTE Confidence: 0.8825603

00:06:41.320 --> 00:06:41.820 three.

NOTE Confidence: 0.8862959

00:06:42.485 --> 00:06:44.585 So these early studies were

NOTE Confidence: 0.8862959

00:06:44.805 --> 00:06:46.825 surgical infarcts, acute delivery

NOTE Confidence: 0.9611542

00:06:47.285 --> 00:06:48.485 in pigs, the pigs were

NOTE Confidence: 0.9611542

00:06:48.485 --> 00:06:49.525 shipped to us, and then

NOTE Confidence: 0.9611542

00:06:49.525 --> 00:06:50.805 we did the imaging with

NOTE Confidence: 0.9611542

00:06:50.805 --> 00:06:52.565 our MMP targeted agent as

NOTE Confidence: 0.9611542

00:06:52.565 --> 00:06:54.105 well as perfusion imaging.

NOTE Confidence: 0.98517925

00:06:55.750 --> 00:06:57.669 And shown here are sort

NOTE Confidence: 0.98517925

00:06:57.669 --> 00:06:58.409 of the early

NOTE Confidence: 0.9497581

00:06:58.710 --> 00:07:00.229 or the initial results here.

NOTE Confidence: 0.9497581

00:07:00.229 --> 00:07:01.689 So shown on top

NOTE Confidence: 0.9687657

00:07:02.069 --> 00:07:02.569 are

NOTE Confidence: 0.9169114

00:07:02.870 --> 00:07:05.189 hearts, control hearts, control hearts,

NOTE Confidence: 0.9169114

00:07:05.189 --> 00:07:06.729 post myocardial infarction

NOTE Confidence: 0.9185284

00:07:07.235 --> 00:07:08.195 and you can see the

NOTE Confidence: 0.9185284

00:07:08.195 --> 00:07:09.795 decreased perfusion area, hearts that

NOTE Confidence: 0.9185284

00:07:09.795 --> 00:07:11.655 were delivered in a hydrogel,

NOTE Confidence: 0.9185284

00:07:11.955 --> 00:07:13.075 and hearts that were delivered

NOTE Confidence: 0.9185284

00:07:13.075 --> 00:07:14.775 a hydrogel that released recombinant

NOTE Confidence: 0.9185284

00:07:14.915 --> 00:07:16.755 TINP three. And below are

NOTE Confidence: 0.9185284

00:07:16.755 --> 00:07:18.035 the MMP maps. You can

NOTE Confidence: 0.9185284

00:07:18.035 --> 00:07:19.235 see at baseline there isn't

NOTE Confidence: 0.9185284

00:07:19.235 --> 00:07:20.595 a lot of MMP activation

NOTE Confidence: 0.9185284

00:07:20.595 --> 00:07:22.050 in the heart. Post MI

NOTE Confidence: 0.9185284

00:07:22.050 --> 00:07:23.729 there's activation in the infarct

NOTE Confidence: 0.9185284

00:07:23.729 --> 00:07:25.490 area, peri infarct area and

NOTE Confidence: 0.9185284

00:07:25.490 --> 00:07:26.530 the atria due to a

NOTE Confidence: 0.9185284

00:07:26.530 --> 00:07:27.990 pressure and volume overload.

NOTE Confidence: 0.9507889

00:07:28.530 --> 00:07:30.370 And the hydrogels themselves have

NOTE Confidence: 0.9507889

00:07:30.370 --> 00:07:32.129 an effect, but local release

NOTE Confidence: 0.9507889

00:07:32.129 --> 00:07:33.729 of an MMP inhibitor totally

NOTE Confidence: 0.9507889

00:07:33.729 --> 00:07:35.270 suppressed MMP activation.

NOTE Confidence: 0.99837184

00:07:36.034 --> 00:07:36.694 And so,

NOTE Confidence: 0.99883705

00:07:37.474 --> 00:07:38.294 shown here

NOTE Confidence: 0.98548424

00:07:38.675 --> 00:07:40.775 is, what we, we demonstrated

NOTE Confidence: 0.9968657

00:07:41.155 --> 00:07:42.375 that we significantly

NOTE Confidence: 0.99613935

00:07:42.914 --> 00:07:43.414 inhibited,

NOTE Confidence: 0.94867325

00:07:44.914 --> 00:07:46.294 the uptake of a compound

NOTE Confidence: 0.94867325

00:07:46.354 --> 00:07:47.634 with the local release and

NOTE Confidence: 0.94867325

00:07:47.634 --> 00:07:48.854 that there was a relationship

NOTE Confidence: 0.99930084

00:07:49.470 --> 00:07:49.970 between

NOTE Confidence: 0.99171895

00:07:50.270 --> 00:07:52.590 suppression of MMPs and changes

NOTE Confidence: 0.99171895

00:07:52.590 --> 00:07:54.450 in regional myocardial function.

NOTE Confidence: 0.9960879

00:07:56.590 --> 00:07:57.230 So now,

NOTE Confidence: 0.9973984

00:07:57.630 --> 00:07:59.490 the next step was to

NOTE Confidence: 0.9973984

00:07:59.550 --> 00:08:00.610 take these hydrogels

NOTE Confidence: 0.94207865

00:08:00.990 --> 00:08:02.850 and we wanna deliver therapies,

NOTE Confidence: 0.94207865

00:08:02.910 --> 00:08:04.430 but we wanted to radio

NOTE Confidence: 0.94207865

00:08:04.430 --> 00:08:05.615 label the drugs so that

NOTE Confidence: 0.94207865

00:08:05.615 --> 00:08:06.815 we not only could track

NOTE Confidence: 0.94207865

00:08:06.815 --> 00:08:08.035 the initial delivery

NOTE Confidence: 0.97724295

00:08:08.495 --> 00:08:09.935 of these hydrogels into the

NOTE Confidence: 0.97724295

00:08:09.935 --> 00:08:11.215 heart, but then we could

NOTE Confidence: 0.97724295

00:08:11.215 --> 00:08:12.195 track the,

NOTE Confidence: 0.98541105

00:08:12.575 --> 00:08:14.195 the, the dispersion and retention

NOTE Confidence: 0.98541105

00:08:14.335 --> 00:08:15.935 of these drugs from the

NOTE Confidence: 0.98541105

00:08:15.935 --> 00:08:16.435 hydrogels

NOTE Confidence: 0.96196145

00:08:16.895 --> 00:08:18.735 and then use molecular imaging

NOTE Confidence: 0.96196145

00:08:18.735 --> 00:08:20.515 to track the therapeutic effects.

NOTE Confidence: 0.91866827

00:08:21.080 --> 00:08:22.380 So again, doxycycline

NOTE Confidence: 0.92723566

00:08:22.760 --> 00:08:24.040 has been shown as a

NOTE Confidence: 0.92723566

00:08:24.040 --> 00:08:25.960 weak MMP inhibitor in clinical

NOTE Confidence: 0.92723566

00:08:25.960 --> 00:08:27.320 trials to have a benefit

NOTE Confidence: 0.92723566

00:08:27.320 --> 00:08:28.940 prevent post infarct remodeling,

NOTE Confidence: 0.9983968

00:08:29.560 --> 00:08:30.760 but we wanted to give

NOTE Confidence: 0.9983968

00:08:30.760 --> 00:08:32.520 high doses locally by this

NOTE Confidence: 0.9983968

00:08:32.520 --> 00:08:33.740 hydrogel approach.

NOTE Confidence: 0.9459639

00:08:35.775 --> 00:08:37.135 So in a small number

NOTE Confidence: 0.9459639

00:08:37.135 --> 00:08:38.655 of animals post MI and

NOTE Confidence: 0.9459639

00:08:38.655 --> 00:08:40.655 control, we delivered these drug

NOTE Confidence: 0.9459639

00:08:40.655 --> 00:08:42.675 delivering hydrogels and demonstrated

NOTE Confidence: 0.9412629

00:08:43.455 --> 00:08:44.975 as shown here in color

NOTE Confidence: 0.9412629

00:08:44.975 --> 00:08:47.775 code the the, delivery and

NOTE Confidence: 0.9412629

00:08:47.775 --> 00:08:50.115 retention over time of the

NOTE Confidence: 0.80237997

00:08:50.459 --> 00:08:51.199 radio labeled,

NOTE Confidence: 0.9290766

00:08:51.660 --> 00:08:53.579 MMP inhibitor on top of

NOTE Confidence: 0.9290766

00:08:53.579 --> 00:08:54.860 a cine CT and we

NOTE Confidence: 0.9290766

00:08:54.860 --> 00:08:56.459 can sort of watch that

NOTE Confidence: 0.9290766

00:08:56.459 --> 00:08:57.759 disperse over time.

NOTE Confidence: 0.931618

00:08:59.420 --> 00:09:00.540 So then we wanted to

NOTE Confidence: 0.931618

00:09:00.540 --> 00:09:01.660 what were the long term

NOTE Confidence: 0.931618

00:09:01.660 --> 00:09:02.939 effects of these drugs, so

NOTE Confidence: 0.931618

00:09:02.939 --> 00:09:04.699 we performed chronic animals. Our

NOTE Confidence: 0.931618

00:09:04.699 --> 00:09:06.195 initial studies were done in

NOTE Confidence: 0.931618

00:09:06.275 --> 00:09:07.175 permanent occlusions,

NOTE Confidence: 0.99269074

00:09:07.795 --> 00:09:08.915 but now we're doing a

NOTE Confidence: 0.99269074

00:09:08.915 --> 00:09:09.415 percutaneous

NOTE Confidence: 0.8365779

00:09:09.795 --> 00:09:11.795 ninety minute balloon occlusion more

NOTE Confidence: 0.8365779

00:09:11.795 --> 00:09:13.235 akin to what happens into

NOTE Confidence: 0.8365779

00:09:13.235 --> 00:09:14.375 pit in in patients.

NOTE Confidence: 0.96647596

00:09:14.755 --> 00:09:16.035 So we have an infarct,

NOTE Confidence: 0.96647596

00:09:16.035 --> 00:09:17.235 and then three days later,

NOTE Confidence: 0.96647596

00:09:17.235 --> 00:09:19.335 we do targeted MMP imaging,

NOTE Confidence: 0.96647596

00:09:19.635 --> 00:09:20.995 and then we do rest

NOTE Confidence: 0.96647596

00:09:20.995 --> 00:09:21.975 and low dose

NOTE Confidence: 0.91222054

00:09:22.329 --> 00:09:22.829 echo,

NOTE Confidence: 0.9406984

00:09:23.370 --> 00:09:25.309 imaging, stress echo imaging.

NOTE Confidence: 0.9620267

00:09:25.850 --> 00:09:26.589 And then,

NOTE Confidence: 0.9478539

00:09:27.050 --> 00:09:28.410 five days later, four days

NOTE Confidence: 0.9478539

00:09:28.410 --> 00:09:30.269 later, we deliver the hydrogels

NOTE Confidence: 0.9478539

00:09:30.490 --> 00:09:31.690 through a more, a small

NOTE Confidence: 0.9478539

00:09:31.690 --> 00:09:33.209 surgical incision and then we

NOTE Confidence: 0.9478539

00:09:33.209 --> 00:09:33.709 reevaluate

NOTE Confidence: 0.9509673

00:09:34.570 --> 00:09:36.010 the animals at two and

NOTE Confidence: 0.9509673

00:09:36.010 --> 00:09:37.000 four weeks. And

NOTE Confidence: 0.9410311

00:09:38.225 --> 00:09:39.665 so shown here are cine

NOTE Confidence: 0.9410311

00:09:39.665 --> 00:09:41.765 CT images of a control,

NOTE Confidence: 0.96596044

00:09:42.225 --> 00:09:43.425 pig, a pig that got

NOTE Confidence: 0.96596044

00:09:43.425 --> 00:09:44.625 the hydrogel and the pig

NOTE Confidence: 0.96596044

00:09:44.625 --> 00:09:45.684 that got the hydrogel

NOTE Confidence: 0.9454633

00:09:45.985 --> 00:09:47.684 that locally released doxycycline.

NOTE Confidence: 0.9560244

00:09:48.465 --> 00:09:49.985 And shown are the bullseye

NOTE Confidence: 0.9560244

00:09:49.985 --> 00:09:51.265 map showing that in the

NOTE Confidence: 0.9560244

00:09:51.265 --> 00:09:53.125 MI controls, there's a significant

NOTE Confidence: 0.952319

00:09:53.700 --> 00:09:55.160 regional activation of MMPs.

NOTE Confidence: 0.97165436

00:09:55.940 --> 00:09:57.480 The delivery of these hydrogels

NOTE Confidence: 0.97165436

00:09:57.700 --> 00:09:59.460 modulated that activation, but the

NOTE Confidence: 0.97165436

00:09:59.460 --> 00:10:01.380 local release of an MMP

NOTE Confidence: 0.97165436

00:10:01.380 --> 00:10:02.520 inhibitor significantly

NOTE Confidence: 0.975509

00:10:02.900 --> 00:10:04.360 suppressed MMP activation.

NOTE Confidence: 0.9836204

00:10:05.059 --> 00:10:06.520 And then this was associated

NOTE Confidence: 0.9836204

00:10:06.740 --> 00:10:07.240 with

NOTE Confidence: 0.9896327

00:10:07.545 --> 00:10:09.725 decreases in left ventricular dilatation,

NOTE Confidence: 0.98731714

00:10:10.265 --> 00:10:12.184 decreases in left ventricular filling

NOTE Confidence: 0.98731714

00:10:12.184 --> 00:10:12.684 pressures,

NOTE Confidence: 0.9992787

00:10:13.625 --> 00:10:14.524 and suppression

NOTE Confidence: 0.9798533

00:10:14.825 --> 00:10:16.184 of the uptake of our

NOTE Confidence: 0.9798533

00:10:16.184 --> 00:10:17.804 MMP targeted radiotracer.

NOTE Confidence: 0.99405575

00:10:19.770 --> 00:10:21.950 So we've also explored another,

NOTE Confidence: 0.9584091

00:10:22.410 --> 00:10:24.110 targeted agent and that

NOTE Confidence: 0.8756107

00:10:24.570 --> 00:10:25.150 is maracyclotide,

NOTE Confidence: 0.945437

00:10:25.530 --> 00:10:27.070 which is an RGT peptide

NOTE Confidence: 0.945437

00:10:27.370 --> 00:10:28.410 that binds to the alpha

NOTE Confidence: 0.945437

00:10:28.410 --> 00:10:30.250 V beta three integrin, which

NOTE Confidence: 0.945437

00:10:30.250 --> 00:10:32.350 is expressed on proliferating endothelial

NOTE Confidence: 0.945437

00:10:32.570 --> 00:10:33.070 cells,

NOTE Confidence: 0.9350743

00:10:33.665 --> 00:10:35.845 and also in inflammatory cells.

NOTE Confidence: 0.9350743

00:10:36.064 --> 00:10:37.425 And so it's, it's thought

NOTE Confidence: 0.9350743

00:10:37.425 --> 00:10:38.505 to be early post amide

NOTE Confidence: 0.9350743

00:10:38.505 --> 00:10:40.004 to be marker of angiogenesis.

NOTE Confidence: 0.9441529

00:10:40.464 --> 00:10:42.064 And these agents were developed

NOTE Confidence: 0.9441529

00:10:42.064 --> 00:10:43.985 as oncological imaging agents and

NOTE Confidence: 0.9441529

00:10:43.985 --> 00:10:45.125 we've sort of adapted,

NOTE Confidence: 0.9944769

00:10:45.504 --> 00:10:47.365 adapted them for cardiac imaging.

NOTE Confidence: 0.90477085

00:10:48.080 --> 00:10:49.520 So again, we created our

NOTE Confidence: 0.90477085

00:10:49.520 --> 00:10:51.040 infarct model. We assessed the

NOTE Confidence: 0.90477085

00:10:51.040 --> 00:10:51.940 area at risk.

NOTE Confidence: 0.8495027

00:10:52.960 --> 00:10:54.000 And then at five days

NOTE Confidence: 0.8495027

00:10:54.000 --> 00:10:54.740 we performed

NOTE Confidence: 0.8812651

00:10:55.120 --> 00:10:56.640 flow imaging with thalene or

NOTE Confidence: 0.8812651

00:10:56.640 --> 00:10:58.320 perfusion imaging and then targeted

NOTE Confidence: 0.8812651

00:10:58.320 --> 00:10:59.380 imaging of angiogenesis.

NOTE Confidence: 0.93953747

00:11:00.215 --> 00:11:02.054 And immediately thereafter through a

NOTE Confidence: 0.93953747

00:11:02.054 --> 00:11:03.975 small surgical window delivered the

NOTE Confidence: 0.93953747

00:11:03.975 --> 00:11:04.475 hydrogels

NOTE Confidence: 0.97274745

00:11:04.934 --> 00:11:06.215 and then looked a week

NOTE Confidence: 0.97274745

00:11:06.215 --> 00:11:07.675 later at angiogenesis

NOTE Confidence: 0.9964665

00:11:08.455 --> 00:11:09.195 and perfusion.

NOTE Confidence: 0.98972034

00:11:11.255 --> 00:11:12.455 And shown here are the

NOTE Confidence: 0.98972034

00:11:12.455 --> 00:11:13.655 three d maps of the

NOTE Confidence: 0.98972034

00:11:13.655 --> 00:11:15.575 perfusion defect in the lateral

NOTE Confidence: 0.98972034

00:11:15.575 --> 00:11:17.230 wall and the focal uptake

NOTE Confidence: 0.98972034

00:11:17.230 --> 00:11:18.910 of this compound that targets

NOTE Confidence: 0.98972034

00:11:18.910 --> 00:11:19.410 angiogenesis.

NOTE Confidence: 0.9969808

00:11:20.510 --> 00:11:21.790 And we showed that giving

NOTE Confidence: 0.9969808

00:11:21.790 --> 00:11:22.529 the hydrogels

NOTE Confidence: 0.98897773

00:11:23.070 --> 00:11:24.769 actually stimulated angiogenesis

NOTE Confidence: 0.9746059

00:11:25.550 --> 00:11:27.410 resulted in less LV dilatation

NOTE Confidence: 0.98467636

00:11:28.029 --> 00:11:29.630 and resulted in improvements in

NOTE Confidence: 0.98467636

00:11:29.630 --> 00:11:31.010 left ventricular function.

NOTE Confidence: 0.96261466

00:11:32.684 --> 00:11:34.545 So when we verified histologically

NOTE Confidence: 0.9846766

00:11:35.084 --> 00:11:36.444 that those changes that we

NOTE Confidence: 0.9846766

00:11:36.444 --> 00:11:37.804 preserved with the imaging were

NOTE Confidence: 0.9846766

00:11:37.804 --> 00:11:38.304 confirmed

NOTE Confidence: 0.9983512

00:11:38.764 --> 00:11:40.384 with markers of angiogenesis

NOTE Confidence: 0.978986

00:11:40.925 --> 00:11:43.324 and integrin activation with very

NOTE Confidence: 0.978986

00:11:43.324 --> 00:11:45.485 little inflammatory response around the

NOTE Confidence: 0.978986

00:11:45.485 --> 00:11:45.985 hydrogels.

NOTE Confidence: 0.93758684

00:11:48.270 --> 00:11:49.630 So now I've showed you

NOTE Confidence: 0.93758684

00:11:49.630 --> 00:11:51.070 surgical delivery, but we want

NOTE Confidence: 0.93758684

00:11:51.070 --> 00:11:52.270 to deliver this in a

NOTE Confidence: 0.93758684

00:11:52.270 --> 00:11:53.870 non invasive way, and so

NOTE Confidence: 0.93758684

00:11:53.870 --> 00:11:55.809 we initially started to use

NOTE Confidence: 0.93758684

00:11:56.110 --> 00:11:56.610 superimposed

NOTE Confidence: 0.9174268

00:11:57.070 --> 00:11:58.670 three d ECHO on our

NOTE Confidence: 0.9174268

00:11:58.670 --> 00:12:00.270 fluoro suite. And then under

NOTE Confidence: 0.9174268

00:12:00.270 --> 00:12:01.570 fluoroscopic guidance,

NOTE Confidence: 0.9786291

00:12:02.395 --> 00:12:03.275 you can see,

NOTE Confidence: 0.99883705

00:12:03.835 --> 00:12:04.335 here

NOTE Confidence: 0.96843606

00:12:04.795 --> 00:12:06.795 a needle being passed, through

NOTE Confidence: 0.96843606

00:12:06.795 --> 00:12:08.154 the chest wall into the

NOTE Confidence: 0.96843606

00:12:08.154 --> 00:12:08.654 myocardium

NOTE Confidence: 0.9924223

00:12:09.115 --> 00:12:10.475 for the delivery of these

NOTE Confidence: 0.9924223

00:12:10.475 --> 00:12:10.975 hydrogels.

NOTE Confidence: 0.9918537

00:12:11.275 --> 00:12:11.934 And then,

NOTE Confidence: 0.9569779

00:12:12.475 --> 00:12:13.355 if we look at the

NOTE Confidence: 0.9569779

00:12:13.355 --> 00:12:15.035 gated images, this is a

NOTE Confidence: 0.9569779

00:12:15.035 --> 00:12:15.535 transesophageal

NOTE Confidence: 0.99350494

00:12:16.075 --> 00:12:17.054 echo at baseline

NOTE Confidence: 0.9804749

00:12:18.000 --> 00:12:19.760 following hydrogel delivery, and you

NOTE Confidence: 0.9804749

00:12:19.760 --> 00:12:21.200 can see the hydrogel within

NOTE Confidence: 0.9804749

00:12:21.200 --> 00:12:22.420 the wall of the heart

NOTE Confidence: 0.8755465

00:12:22.880 --> 00:12:24.559 and then, an hour post

NOTE Confidence: 0.8755465

00:12:24.559 --> 00:12:25.059 delivery.

NOTE Confidence: 0.9390222

00:12:26.000 --> 00:12:27.040 But we found that that

NOTE Confidence: 0.9390222

00:12:27.040 --> 00:12:28.000 was not the best way,

NOTE Confidence: 0.9390222

00:12:28.000 --> 00:12:29.040 so now we wanna do

NOTE Confidence: 0.9390222

00:12:29.040 --> 00:12:29.540 multimodality

NOTE Confidence: 0.9704065

00:12:30.080 --> 00:12:31.565 delivery of these agents and,

NOTE Confidence: 0.9704065

00:12:31.565 --> 00:12:32.684 and what we made the

NOTE Confidence: 0.9704065

00:12:32.684 --> 00:12:34.304 observation that early post

NOTE Confidence: 0.925237

00:12:34.845 --> 00:12:36.684 MI, there's calcium deposition and

NOTE Confidence: 0.925237

00:12:36.684 --> 00:12:38.285 that calcium can be detected

NOTE Confidence: 0.925237

00:12:38.285 --> 00:12:39.105 on the CT

NOTE Confidence: 0.9079793

00:12:39.644 --> 00:12:41.245 within three to five days

NOTE Confidence: 0.9079793

00:12:41.245 --> 00:12:43.005 post MI. And it appears

NOTE Confidence: 0.9079793

00:12:43.005 --> 00:12:44.605 that a hyperdensity on non

NOTE Confidence: 0.9079793

00:12:44.605 --> 00:12:46.125 contrast studies and an increased

NOTE Confidence: 0.9079793

00:12:46.125 --> 00:12:47.540 density on on late hyper

NOTE Confidence: 0.9079793

00:12:47.540 --> 00:12:48.520 enhanced studies.

NOTE Confidence: 0.9767283

00:12:49.059 --> 00:12:50.260 So we use that to

NOTE Confidence: 0.9767283

00:12:50.260 --> 00:12:52.020 guide the delivery. So we

NOTE Confidence: 0.9767283

00:12:52.020 --> 00:12:53.860 took a sixty four slice

NOTE Confidence: 0.9767283

00:12:53.860 --> 00:12:54.840 CT scanner.

NOTE Confidence: 0.93475956

00:12:55.380 --> 00:12:57.300 We outlined the area of

NOTE Confidence: 0.93475956

00:12:57.300 --> 00:12:58.679 the hyper density

NOTE Confidence: 0.95602566

00:12:59.315 --> 00:13:01.075 and then registered that with

NOTE Confidence: 0.95602566

00:13:01.075 --> 00:13:02.355 a cone beam CT in

NOTE Confidence: 0.95602566

00:13:02.355 --> 00:13:03.714 the fluoro unit. So we

NOTE Confidence: 0.95602566

00:13:03.714 --> 00:13:04.855 have a a

NOTE Confidence: 0.81871784

00:13:05.235 --> 00:13:05.894 low resolution

NOTE Confidence: 0.9986286

00:13:06.274 --> 00:13:06.774 CT

NOTE Confidence: 0.9473764

00:13:07.154 --> 00:13:08.515 in the fluoro space. Now

NOTE Confidence: 0.9473764

00:13:08.515 --> 00:13:10.355 we're in fluoro, we're moving

NOTE Confidence: 0.9473764

00:13:10.355 --> 00:13:12.054 in three d CT space.

NOTE Confidence: 0.9473764

00:13:12.355 --> 00:13:13.095 And so

NOTE Confidence: 0.89159924

00:13:13.449 --> 00:13:15.370 under that fluoroscopic guidance, we

NOTE Confidence: 0.89159924

00:13:15.370 --> 00:13:17.790 placed guide needles, parasternal directed

NOTE Confidence: 0.89159924

00:13:18.009 --> 00:13:19.529 into the target into the

NOTE Confidence: 0.89159924

00:13:19.529 --> 00:13:20.589 infarct area.

NOTE Confidence: 0.9993712

00:13:21.290 --> 00:13:22.029 And then

NOTE Confidence: 0.9512457

00:13:22.649 --> 00:13:23.389 as before,

NOTE Confidence: 0.9988299

00:13:24.649 --> 00:13:25.309 we did

NOTE Confidence: 0.86752623

00:13:26.654 --> 00:13:27.154 transesophageal,

NOTE Confidence: 0.99692637

00:13:28.334 --> 00:13:28.834 echo

NOTE Confidence: 0.9982313

00:13:29.214 --> 00:13:29.954 to verify

NOTE Confidence: 0.86110646

00:13:30.255 --> 00:13:32.334 that a steerable meter needle

NOTE Confidence: 0.86110646

00:13:32.334 --> 00:13:34.095 passed through these guides was

NOTE Confidence: 0.86110646

00:13:34.095 --> 00:13:35.795 placed mid myocardial before

NOTE Confidence: 0.96306527

00:13:36.175 --> 00:13:37.855 we delivered the hydrogel. So

NOTE Confidence: 0.96306527

00:13:37.855 --> 00:13:39.930 now we've developed a percutaneous

NOTE Confidence: 0.96306527

00:13:40.230 --> 00:13:42.070 non invasive way to deliver

NOTE Confidence: 0.96306527

00:13:42.070 --> 00:13:44.070 these therapeutic hydrogels to the

NOTE Confidence: 0.96306527

00:13:44.070 --> 00:13:45.530 central infarct area.

NOTE Confidence: 0.9873153

00:13:46.870 --> 00:13:48.550 And this just shows our,

NOTE Confidence: 0.9873153

00:13:48.950 --> 00:13:50.250 ability to effectively

NOTE Confidence: 0.9507788

00:13:50.790 --> 00:13:53.110 deliver these iodinated hydrogels into

NOTE Confidence: 0.9507788

00:13:53.110 --> 00:13:55.005 the central infarct area. And

NOTE Confidence: 0.9507788

00:13:55.085 --> 00:13:56.545 then, of course, we're evaluating

NOTE Confidence: 0.9507788

00:13:56.765 --> 00:13:58.365 that with a number of

NOTE Confidence: 0.9507788

00:13:58.365 --> 00:14:00.445 targeted molecular probes, looking at

NOTE Confidence: 0.9507788

00:14:00.445 --> 00:14:02.545 MMP activation, looking at fibroblast

NOTE Confidence: 0.9507788

00:14:02.765 --> 00:14:03.265 activation,

NOTE Confidence: 0.9995095

00:14:03.725 --> 00:14:05.665 and other markers of inflammation.

NOTE Confidence: 0.9993857

00:14:07.980 --> 00:14:08.480 So

NOTE Confidence: 0.9743833

00:14:09.100 --> 00:14:11.100 we also have been working

NOTE Confidence: 0.9743833

00:14:11.100 --> 00:14:13.100 to develop a novel catheter

NOTE Confidence: 0.9743833

00:14:13.100 --> 00:14:14.720 based approach to do molecular

NOTE Confidence: 0.9743833

00:14:14.780 --> 00:14:16.640 guided therapy. So in cardiology,

NOTE Confidence: 0.9743833

00:14:16.780 --> 00:14:18.300 a standard approach is to

NOTE Confidence: 0.9743833

00:14:18.300 --> 00:14:20.380 do electro anatomical mapping that

NOTE Confidence: 0.9743833

00:14:20.380 --> 00:14:21.600 is passing a catheter

NOTE Confidence: 0.9838073

00:14:21.935 --> 00:14:23.855 and mapping electrical voltages on

NOTE Confidence: 0.9838073

00:14:23.855 --> 00:14:25.154 the surface of the heart.

NOTE Confidence: 0.9838073

00:14:25.454 --> 00:14:27.055 So in collaboration with a

NOTE Confidence: 0.9838073

00:14:27.055 --> 00:14:28.514 company in in California,

NOTE Confidence: 0.9741436

00:14:29.135 --> 00:14:30.975 we replaced that electrical sensor

NOTE Confidence: 0.9741436

00:14:30.975 --> 00:14:32.654 with a plastic scintillator to

NOTE Confidence: 0.9741436

00:14:32.654 --> 00:14:34.035 detect local radiation.

NOTE Confidence: 0.9936348

00:14:34.550 --> 00:14:36.310 So radio tracers that emit

NOTE Confidence: 0.9936348

00:14:36.310 --> 00:14:37.829 betas will will travel one

NOTE Confidence: 0.9936348

00:14:37.829 --> 00:14:38.949 or two millimeters. So on

NOTE Confidence: 0.9936348

00:14:38.949 --> 00:14:40.069 the tip of the catheter,

NOTE Confidence: 0.9936348

00:14:40.069 --> 00:14:40.970 we can detect

NOTE Confidence: 0.97080237

00:14:41.350 --> 00:14:43.509 a targeted molecular signal. Now

NOTE Confidence: 0.97080237

00:14:43.509 --> 00:14:44.550 many of the probes, as

NOTE Confidence: 0.97080237

00:14:44.550 --> 00:14:46.089 you know, deliver an imageable

NOTE Confidence: 0.97080237

00:14:46.149 --> 00:14:47.775 gamma as well as a

NOTE Confidence: 0.97080237

00:14:47.775 --> 00:14:49.135 low energy beta. So we

NOTE Confidence: 0.97080237

00:14:49.135 --> 00:14:50.175 can have a three d

NOTE Confidence: 0.97080237

00:14:50.175 --> 00:14:52.095 map of the of the

NOTE Confidence: 0.97080237

00:14:52.095 --> 00:14:54.015 radio tracer by gamma imaging

NOTE Confidence: 0.97080237

00:14:54.015 --> 00:14:55.315 and then local detection,

NOTE Confidence: 0.97252035

00:14:56.175 --> 00:14:58.095 with this beta detector. And

NOTE Confidence: 0.97252035

00:14:58.095 --> 00:14:58.975 we have a number of

NOTE Confidence: 0.97252035

00:14:58.975 --> 00:15:00.255 versions of that, and this

NOTE Confidence: 0.97252035

00:15:00.255 --> 00:15:01.315 is sort of a patented

NOTE Confidence: 0.97252035

00:15:01.455 --> 00:15:01.955 technology.

NOTE Confidence: 0.9546728

00:15:03.260 --> 00:15:04.140 And the last thing we

NOTE Confidence: 0.9546728

00:15:04.140 --> 00:15:05.260 wanna talk about is the

NOTE Confidence: 0.9546728

00:15:05.260 --> 00:15:06.700 use of this approach in

NOTE Confidence: 0.9546728

00:15:06.700 --> 00:15:08.220 lung injury models. And so

NOTE Confidence: 0.9546728

00:15:08.220 --> 00:15:09.820 again, we apply the same

NOTE Confidence: 0.9546728

00:15:09.820 --> 00:15:11.580 approach where we take, a

NOTE Confidence: 0.9546728

00:15:11.580 --> 00:15:13.260 CT scan, we define the

NOTE Confidence: 0.9546728

00:15:13.260 --> 00:15:13.760 airways,

NOTE Confidence: 0.97719383

00:15:14.460 --> 00:15:15.740 and then we register that

NOTE Confidence: 0.97719383

00:15:15.740 --> 00:15:17.260 with a cone beam CT

NOTE Confidence: 0.97719383

00:15:17.260 --> 00:15:18.400 and then under fluoroscopic

NOTE Confidence: 0.9671529

00:15:18.714 --> 00:15:20.255 guidance with a balloon catheter,

NOTE Confidence: 0.9730013

00:15:20.714 --> 00:15:21.935 we deliver bleomycin,

NOTE Confidence: 0.9688634

00:15:22.315 --> 00:15:24.395 a lung toxic agent. So

NOTE Confidence: 0.9688634

00:15:24.395 --> 00:15:25.595 we can create a lung

NOTE Confidence: 0.9688634

00:15:25.595 --> 00:15:27.515 injury model, and then we

NOTE Confidence: 0.9688634

00:15:27.515 --> 00:15:29.274 perform serial imaging with a

NOTE Confidence: 0.9688634

00:15:29.274 --> 00:15:30.815 number of molecular probes.

NOTE Confidence: 0.8697712

00:15:31.340 --> 00:15:32.780 And shown is here is

NOTE Confidence: 0.8697712

00:15:32.780 --> 00:15:33.280 just

NOTE Confidence: 0.9545

00:15:34.140 --> 00:15:36.060 SPECT imaging of our our

NOTE Confidence: 0.9545

00:15:36.060 --> 00:15:37.500 tech labeled agent looks at

NOTE Confidence: 0.9545

00:15:37.500 --> 00:15:39.660 fiberglass activation protein to look

NOTE Confidence: 0.9545

00:15:39.660 --> 00:15:41.100 at the early markers of

NOTE Confidence: 0.9545

00:15:41.100 --> 00:15:41.600 fibrosis.

NOTE Confidence: 0.9611623

00:15:42.380 --> 00:15:43.900 And clearly, there was increased

NOTE Confidence: 0.9611623

00:15:43.900 --> 00:15:45.360 uptake relative to

NOTE Confidence: 0.97243464

00:15:45.855 --> 00:15:46.755 remote areas.

NOTE Confidence: 0.98107195

00:15:47.774 --> 00:15:48.675 So to summarize,

NOTE Confidence: 0.9974147

00:15:49.695 --> 00:15:50.755 molecular imaging

NOTE Confidence: 0.9944974

00:15:51.214 --> 00:15:52.575 is critical for the early

NOTE Confidence: 0.9944974

00:15:52.575 --> 00:15:53.955 detection of the disease,

NOTE Confidence: 0.97749496

00:15:55.295 --> 00:15:56.595 and that we're exploring

NOTE Confidence: 0.94047374

00:15:56.975 --> 00:15:58.015 the, the use of these

NOTE Confidence: 0.94047374

00:15:58.015 --> 00:16:00.390 thyranostic hydrogels that allow us

NOTE Confidence: 0.94047374

00:16:00.470 --> 00:16:02.330 to deliver concentrated drugs

NOTE Confidence: 0.9393704

00:16:02.790 --> 00:16:04.630 or cells or gene therapy

NOTE Confidence: 0.9393704

00:16:04.630 --> 00:16:06.170 to the heart to modulate

NOTE Confidence: 0.9393704

00:16:06.310 --> 00:16:07.690 post infarct prepare

NOTE Confidence: 0.8984788

00:16:08.150 --> 00:16:09.530 or other cardio, cardiovascular

NOTE Confidence: 0.76470345

00:16:09.990 --> 00:16:10.490 processes.

NOTE Confidence: 0.96270585

00:16:10.950 --> 00:16:12.570 And we're exploring these therapies

NOTE Confidence: 0.96270585

00:16:12.630 --> 00:16:13.750 also in the setting of

NOTE Confidence: 0.96270585

00:16:13.750 --> 00:16:14.570 lung entry.

NOTE Confidence: 0.9747609

00:16:15.485 --> 00:16:16.925 But you need to have

NOTE Confidence: 0.9747609

00:16:16.925 --> 00:16:19.005 molecular imaging to evaluate the

NOTE Confidence: 0.9747609

00:16:19.005 --> 00:16:21.185 therapeutic efficacy of these therapies.

NOTE Confidence: 0.9747609

00:16:21.404 --> 00:16:22.785 And so it's the integration

NOTE Confidence: 0.9747609

00:16:23.005 --> 00:16:24.785 of the theranostics and molecular

NOTE Confidence: 0.9747609

00:16:25.005 --> 00:16:25.505 imaging.

NOTE Confidence: 0.96900153

00:16:26.205 --> 00:16:27.084 And so none of this

NOTE Confidence: 0.96900153

00:16:27.084 --> 00:16:28.445 work would be accomplished without

NOTE Confidence: 0.96900153

00:16:28.445 --> 00:16:29.904 a long list of collaborators

NOTE Confidence: 0.9988149

00:16:30.510 --> 00:16:31.490 here at Yale

NOTE Confidence: 0.88767445

00:16:32.030 --> 00:16:34.450 and within the the YTREC,

NOTE Confidence: 0.9397762

00:16:35.390 --> 00:16:37.230 center as well as other

NOTE Confidence: 0.9397762

00:16:37.230 --> 00:16:39.330 members in cardiology and pathology

NOTE Confidence: 0.9397762

00:16:39.550 --> 00:16:40.290 and radiology,

NOTE Confidence: 0.88416386

00:16:41.230 --> 00:16:42.990 and particularly Stephanie Thorn who's

NOTE Confidence: 0.88416386

00:16:42.990 --> 00:16:44.190 the associate director in the

NOTE Confidence: 0.88416386

00:16:44.190 --> 00:16:45.470 lab and Jim Duncan and

NOTE Confidence: 0.88416386

00:16:45.470 --> 00:16:46.982 Chi Lu. So thank you

NOTE Confidence: 0.88416386

00:16:46.982 --> 00:16:47.802 for your

NOTE Confidence: 0.9980995

00:16:50.982 --> 00:16:51.482 attention.