WEBVTT

00:00:00.000 --> 00:00:02.952 Our next speaker will take neuroimaging

00:00:02.952 --> 00:00:05.719 in a completely different direction.

00:00:05.719 --> 00:00:07.498 Doctor Zachary Corbin,

00:00:07.500 --> 00:00:08.876 assistant professor of neurology,

00:00:08.876 --> 00:00:10.596 head of the Neuron Oncology

00:00:10.596 --> 00:00:11.370 Fellowship program.

00:00:11.370 --> 00:00:13.280 We'll be talking about neuroimaging

00:00:13.280 --> 00:00:14.768 and cancer. Thanks come on up.

00:00:26.880 --> 00:00:27.910 So thank you very much.

00:00:27.910 --> 00:00:29.080 It's really an honor and a

00:00:29.127 --> 00:00:30.849 privilege to be here. I'm Zach Corbin.

00:00:30.849 --> 00:00:33.220 I'm one of the neuro oncologist at Smilo,

00:00:33.220 --> 00:00:35.390 and I'm here to talk about metabolic

00:00:35.390 --> 00:00:36.976 imaging techniques using PET and

NOTE Confidence: 0.886209168571429

00:00:36.976 --> 00:00:38.466 Mr spectroscopy and brain tumors.

NOTE Confidence: 0.886209168571429

00:00:38.470 --> 00:00:40.444 I'd like to start by talking about.

NOTE Confidence: 0.886209168571429

00:00:40.450 --> 00:00:43.711 I can start by talking about the disease.

NOTE Confidence: 0.886209168571429

00:00:43.711 --> 00:00:45.637 We've directed a lot of our

NOTE Confidence: 0.886209168571429

00:00:45.637 --> 00:00:47.746 techniques to which is glioma and

NOTE Confidence: 0.886209168571429

00:00:47.746 --> 00:00:49.190 glioma is surprisingly common.

NOTE Confidence: 0.886209168571429

00:00:49.190 --> 00:00:51.670 I think to most people it's second most

NOTE Confidence: 0.886209168571429

00:00:51.670 --> 00:00:53.748 common type of primary brain tumor.

NOTE Confidence: 0.886209168571429

00:00:53.750 --> 00:00:57.106 US annual instance is 19,000 /.

NOTE Confidence: 0.886209168571429

00:00:57.106 --> 00:00:59.542 12,000 of these are the most aggressive

NOTE Confidence: 0.886209168571429

00:00:59.542 --> 00:01:02.022 and probably most famous glioma which

NOTE Confidence: 0.886209168571429

00:01:02.022 --> 00:01:04.572 is glioblastoma and despite a great

NOTE Confidence: 0.886209168571429

00:01:04.572 --> 00:01:07.044 deal of research and clinical efforts,

NOTE Confidence: 0.886209168571429

00:01:07.050 --> 00:01:08.736 it's a very morbid and mortal.

NOTE Confidence: 0.886209168571429

00:01:08.740 --> 00:01:10.588 Disease where over just over one

2

NOTE Confidence: 0.886209168571429

00:01:10.588 --> 00:01:12.570 in 20 patients at five years,

NOTE Confidence: 0.886209168571429

00:01:12.570 --> 00:01:14.762 remains alive, about 6.8%.

NOTE Confidence: 0.886209168571429

00:01:14.762 --> 00:01:18.462 At last measurement we'll blastoma is

NOTE Confidence: 0.886209168571429

00:01:18.462 --> 00:01:21.198 defined histopathologically with necrosis,

NOTE Confidence: 0.886209168571429

00:01:21.200 --> 00:01:22.815 which is also surrounded by

NOTE Confidence: 0.886209168571429

00:01:22.815 --> 00:01:23.784 pseudo Palisades here,

NOTE Confidence: 0.886209168571429

00:01:23.790 --> 00:01:25.548 and there's lots of nuclear changes,

NOTE Confidence: 0.886209168571429

00:01:25.550 --> 00:01:27.238 and you can see the cells look quite

NOTE Confidence: 0.886209168571429

00:01:27.238 --> 00:01:28.648 different on this microscope slide,

NOTE Confidence: 0.886209168571429

00:01:28.650 --> 00:01:29.850 and these are blood vessels.

NOTE Confidence: 0.886209168571429

00:01:29.850 --> 00:01:31.510 There's blood vessel proliferation.

NOTE Confidence: 0.886209168571429

00:01:31.510 --> 00:01:33.585 We're interested in applying metabolic

NOTE Confidence: 0.886209168571429

00:01:33.585 --> 00:01:35.465 imaging to the treatment of wheel

NOTE Confidence: 0.886209168571429

00:01:35.465 --> 00:01:37.356 blastoma and glioma in general because

NOTE Confidence: 0.886209168571429

00:01:37.356 --> 00:01:38.982 the glioblastoma, for example,

NOTE Confidence: 0.886209168571429

00:01:38.982 --> 00:01:41.719 is treated with a basis of MRI.

NOTE Confidence: 0.886209168571429

00:01:41.720 --> 00:01:42.980 MRI is a diagnosis.

NOTE Confidence: 0.886209168571429

00:01:42.980 --> 00:01:44.555 Patients are treated with surgery

NOTE Confidence: 0.886209168571429

00:01:44.555 --> 00:01:46.636 and then an MRI is performed again,

NOTE Confidence: 0.886209168571429

00:01:46.640 --> 00:01:48.566 postoperatively and then often within a

NOTE Confidence: 0.886209168571429

00:01:48.566 --> 00:01:51.297 month prior to the first phase of treatment,

NOTE Confidence: 0.886209168571429

00:01:51.300 --> 00:01:52.524 which is chemoradiation.

NOTE Confidence: 0.886209168571429

00:01:52.524 --> 00:01:54.972 Another MRI is performed and then

NOTE Confidence: 0.886209168571429

00:01:54.972 --> 00:01:56.778 actually after chemo radiation,

NOTE Confidence: 0.886209168571429

00:01:56.780 --> 00:01:58.940 which lasts about 1 1/2 months.

NOTE Confidence: 0.886209168571429

00:01:58.940 --> 00:02:00.264 One month of break.

NOTE Confidence: 0.886209168571429

00:02:00.264 --> 00:02:02.250 There's another MRI and we actually.

NOTE Confidence: 0.886209168571429

00:02:02.250 --> 00:02:04.335 Perform MRI's every two months

NOTE Confidence: 0.886209168571429

00:02:04.335 --> 00:02:06.003 during the adjuvant chemoradiation

NOTE Confidence: 0.886209168571429

00:02:06.003 --> 00:02:08.128 phase or sorry chemotherapy phase.

NOTE Confidence: 0.886209168571429

00:02:08.130 --> 00:02:10.074 So the average patient often receives

NOTE Confidence: 0.886209168571429

00:02:10.074 --> 00:02:12.720 about a dozen MRI's and this is a

NOTE Confidence: 0.886209168571429

00:02:12.720 --> 00:02:15.145 great opportunity for us to add to

NOTE Confidence: 0.886209168571429

00:02:15.145 --> 00:02:16.998 the patients care in order to tell

NOTE Confidence: 0.886209168571429

00:02:16.998 --> 00:02:18.871 you a little bit about why we would

NOTE Confidence: 0.886209168571429

00:02:18.871 --> 00:02:20.316 use metabolic imaging and glioma.

NOTE Confidence: 0.886209168571429

00:02:20.320 --> 00:02:22.700 So the Warburg effect is the most

NOTE Confidence: 0.886209168571429

00:02:22.700 --> 00:02:24.304 famous metabolic change and it's

NOTE Confidence: 0.886209168571429

00:02:24.304 --> 00:02:25.568 associated with aggressive tumors

NOTE Confidence: 0.886209168571429

00:02:25.568 --> 00:02:27.374 and in order to demonstrate it I'm

NOTE Confidence: 0.886209168571429

00:02:27.374 --> 00:02:29.035 going to show you a diagram where

NOTE Confidence: 0.886209168571429

00:02:29.035 --> 00:02:30.743 this is the outside of the cell.

NOTE Confidence: 0.886209168571429

00:02:30.750 --> 00:02:32.269 This is the inside of the cell.

NOTE Confidence: 0.886209168571429

00:02:32.270 --> 00:02:33.848 So glucose comes into the cell,

NOTE Confidence: 0.886209168571429

00:02:33.850 --> 00:02:35.038 it becomes pyruvate,

NOTE Confidence: 0.886209168571429

00:02:35.038 --> 00:02:37.018 and then there's a dichotomy

NOTE Confidence: 0.886209168571429

00:02:37.018 --> 00:02:38.430 where in general,

NOTE Confidence: 0.886209168571429

00:02:38.430 --> 00:02:40.290 in normal oxygen tension and

NOTE Confidence: 0.886209168571429

00:02:40.290 --> 00:02:41.406 through oxidative phosphorylation

NOTE Confidence: 0.886209168571429

00:02:41.406 --> 00:02:42.610 as mediated through.

NOTE Confidence: 0.886209168571429

00:02:42.610 --> 00:02:44.870 This is my mitochondria cartoon.

NOTE Confidence: 0.886209168571429

00:02:44.870 --> 00:02:47.534 You can see that CO2 evolves and is

NOTE Confidence: 0.886209168571429

00:02:47.534 --> 00:02:49.869 exchanged with bicarbonate and cytosol,

NOTE Confidence: 0.886209168571429

00:02:49.870 --> 00:02:52.505 alternatively usually in low oxygenation

NOTE Confidence: 0.886209168571429

00:02:52.505 --> 00:02:54.613 you'd have glycolysis performed,

NOTE Confidence: 0.886209168571429

00:02:54.620 --> 00:02:55.853 which involves lactate,

NOTE Confidence: 0.886209168571429

00:02:55.853 --> 00:02:57.086 which is acidic,

NOTE Confidence: 0.886209168571429

00:02:57.090 --> 00:02:59.262 and Warburg effect dictates that in

NOTE Confidence: 0.886209168571429

00:02:59.262 --> 00:03:01.710 the presence of normal oxygen tension,

NOTE Confidence: 0.886209168571429

00:03:01.710 --> 00:03:03.775 actually the right side of this diagram.

NOTE Confidence: 0.886209168571429

00:03:03.780 --> 00:03:04.488 Is favored,

NOTE Confidence: 0.886209168571429

00:03:04.488 --> 00:03:06.258 and actually tumors prefer to

NOTE Confidence: 0.886209168571429

00:03:06.258 --> 00:03:08.258 produce the lack produce lactate

NOTE Confidence: 0.886209168571429

00:03:08.258 --> 00:03:10.006 through the Warburg effect.

NOTE Confidence: 0.886209168571429

00:03:10.010 --> 00:03:12.440 So what I'm describing today are

NOTE Confidence: 0.886209168571429

00:03:12.440 --> 00:03:14.060 clinically available techniques to

NOTE Confidence: 0.886209168571429

00:03:14.123 --> 00:03:16.298 actually measure the Warburg effect.

NOTE Confidence: 0.886209168571429

00:03:16.300 --> 00:03:18.876 So Pat has been used in his famous

NOTE Confidence: 0.886209168571429

00:03:18.876 --> 00:03:20.919 as reviewed by Doctor Constable

NOTE Confidence: 0.886209168571429

00:03:20.920 --> 00:03:22.970 for many different radio ligands,

NOTE Confidence: 0.886209168571429

00:03:22.970 --> 00:03:25.120 fluorodeoxyglucose or FDG PET is

NOTE Confidence: 0.886209168571429

00:03:25.120 --> 00:03:27.270 the most common clinical tool.

NOTE Confidence: 0.800555637777778

00:03:27.270 --> 00:03:30.035 And with FDG pet, when we provided

NOTE Confidence: 0.800555637777778

00:03:30.035 --> 00:03:32.558 in the bloodstream of the patient

NOTE Confidence: 0.800555637777778

00:03:32.558 --> 00:03:34.653 it is phosphorylated into FDG.

NOTE Confidence: 0.800555637777778

00:03:34.660 --> 00:03:36.610 Inside the cell, but doesn't actually

NOTE Confidence: 0.800555637777778

00:03:36.610 --> 00:03:39.243 further used by the cell and really

NOTE Confidence: 0.800555637777778

00:03:39.243 --> 00:03:40.939 represents total glucose metabolism,

NOTE Confidence: 0.800555637777778

00:03:40.940 --> 00:03:43.040 but total glucose metabolism in this context

NOTE Confidence: 0.800555637777778

00:03:43.040 --> 00:03:45.636 is a rough characterization of oxidative

NOTE Confidence: 0.800555637777778

00:03:45.636 --> 00:03:47.820 phosphorylation without the specificity,

NOTE Confidence: 0.800555637777778

00:03:47.820 --> 00:03:50.165 so the specificity in our technique comes

NOTE Confidence: 0.800555637777778

00:03:50.165 --> 00:03:52.000 from another clinically available tool,

NOTE Confidence: 0.800555637777778

00:03:52.000 --> 00:03:53.960 which is Mr Spectroscopy,

NOTE Confidence: 0.800555637777778

00:03:53.960 --> 00:03:55.812 NMR spectroscopy, and in this case,

NOTE Confidence: 0.800555637777778

00:03:55.812 --> 00:03:56.530 emerse, spectroscopy.

NOTE Confidence: 0.800555637777778

00:03:56.530 --> 00:03:59.030 NMR, spectroscopic imaging using proton

NOTE Confidence: 0.800555637777778

00:03:59.030 --> 00:04:01.750 based methods can highlight lactate as

NOTE Confidence: 0.800555637777778

00:04:01.750 --> 00:04:04.366 well as other other molecules in the cell.

NOTE Confidence: 0.800555637777778

00:04:04.370 --> 00:04:06.368 And as a representative of mythologist.

NOTE Confidence: 0.800555637777778

00:04:06.370 --> 00:04:09.286 So as a part of my wife CIO award,

NOTE Confidence: 0.800555637777778

00:04:09.290 --> 00:04:11.292 we actually developed a technique in which

NOTE Confidence: 0.800555637777778

00:04:11.292 --> 00:04:13.239 we have labeled it the Warburg index.

NOTE Confidence: 0.800555637777778

00:04:13.240 --> 00:04:15.130 This is actually created at Yale

NOTE Confidence: 0.800555637777778

00:04:15.130 --> 00:04:17.228 and we actually are using lactate

NOTE Confidence: 0.800555637777778

00:04:17.228 --> 00:04:19.544 measured by Mr spectroscopy over SUV,

NOTE Confidence: 0.800555637777778

00:04:19.550 --> 00:04:21.450 which is standard uptake value

NOTE Confidence: 0.800555637777778

00:04:21.450 --> 00:04:22.590 measured by PET,

NOTE Confidence: 0.800555637777778

00:04:22.590 --> 00:04:24.606 to show the Warburg index and

NOTE Confidence: 0.800555637777778

00:04:24.606 --> 00:04:25.950 the Warburg Index works.

NOTE Confidence: 0.800555637777778

00:04:25.950 --> 00:04:27.830 So this is one of my patients in

NOTE Confidence: 0.800555637777778

00:04:27.830 --> 00:04:29.373 this protocol who has a glioblastoma

NOTE Confidence: 0.800555637777778

00:04:29.373 --> 00:04:30.903 and this is the tumor here.

NOTE Confidence: 0.800555637777778

00:04:30.910 --> 00:04:32.134 As you can see,

NOTE Confidence: 0.800555637777778

00:04:32.134 --> 00:04:33.664 causes changes to the brain,

NOTE Confidence: 0.800555637777778

00:04:33.670 --> 00:04:35.068 but I think that the Warburg.

NOTE Confidence: 0.800555637777778

00:04:35.070 --> 00:04:36.505 Index actually really does an

NOTE Confidence: 0.800555637777778

00:04:36.505 --> 00:04:37.940 amazing job of highlighting the

NOTE Confidence: 0.800555637777778

00:04:37.988 --> 00:04:39.324 metabolic derangement that was

NOTE Confidence: 0.800555637777778

00:04:39.324 --> 00:04:40.994 actually occurring in this tumor.

NOTE Confidence: 0.800555637777778

00:04:41.000 --> 00:04:43.328 So you can see blue is relatively normal

NOTE Confidence: 0.800555637777778

00:04:43.328 --> 00:04:45.159 metabolism of the surrounding brain,

NOTE Confidence: 0.800555637777778

00:04:45.160 --> 00:04:47.992 and the red indicates a high Warburg effect

NOTE Confidence: 0.800555637777778

00:04:47.992 --> 00:04:50.995 or high High warberg index in this case.

NOTE Confidence: 0.800555637777778

00:04:51.000 --> 00:04:52.360 In order to talk a little bit about

NOTE Confidence: 0.800555637777778

00:04:52.360 --> 00:04:53.859 why this might teach us about Juliana,

NOTE Confidence: 0.800555637777778

00:04:53.860 --> 00:04:54.110 though,

NOTE Confidence: 0.800555637777778

00:04:54.110 --> 00:04:55.860 I'm going to introduce another thing which

NOTE Confidence: 0.800555637777778

00:04:55.860 --> 00:04:57.745 is called the ISIS history dehydrogenase

NOTE Confidence: 0.800555637777778

00:04:57.745 --> 00:04:59.416 mutation, otherwise known as I.

NOTE Confidence: 0.800555637777778

00:04:59.416 --> 00:05:02.400 DHIDH is used and known in other tumors,

NOTE Confidence: 0.800555637777778

00:05:02.400 --> 00:05:04.296 but in glioma family it is.

NOTE Confidence: 0.800555637777778

00:05:04.300 --> 00:05:05.872 It defines a characteristic,

NOTE Confidence: 0.800555637777778

00:05:05.872 --> 00:05:08.230 and it really begins as discussing

10

00:05:08.297 --> 00:05:10.418 what IH does in the standard cell.

00:05:10.420 --> 00:05:12.724 So I H and the standard cell changes

00:05:12.724 --> 00:05:14.519 isocitrate to alphabetically rate,

00:05:14.520 --> 00:05:16.716 and that is actually a mediator

00:05:16.716 --> 00:05:17.814 in normal metabolism.

00:05:17.820 --> 00:05:19.820 But in an IDH mutant,

00:05:19.820 --> 00:05:20.786 there's a heterodimer.

00:05:20.786 --> 00:05:22.074 Formed, which produces what's

00:05:22.074 --> 00:05:23.610 called an ankle metabolite.

00:05:23.610 --> 00:05:25.041 That accountability is

00:05:25.041 --> 00:05:26.949 named 2 hydroxy glutarate.

00:05:26.950 --> 00:05:28.672 That's not as important to remember

00:05:28.672 --> 00:05:30.230 that this causes downstream changes,

00:05:30.230 --> 00:05:32.410 either directly or otherwise in

00:05:32.410 --> 00:05:34.590 methylation of the genome methylation

00:05:34.656 --> 00:05:36.486 of histones and actually patients

NOTE Confidence: 0.800555637777778

00:05:36.486 --> 00:05:38.830 do better who have these tumors.

NOTE Confidence: 0.800555637777778

00:05:38.830 --> 00:05:39.966 The tumors grow less,

NOTE Confidence: 0.800555637777778

00:05:39.966 --> 00:05:41.670 So what we are proposing is

NOTE Confidence: 0.800555637777778

00:05:41.735 --> 00:05:43.127 that the Warburg effect,

NOTE Confidence: 0.800555637777778

00:05:43.130 --> 00:05:45.116 which otherwise as I showed you

NOTE Confidence: 0.800555637777778

00:05:45.116 --> 00:05:47.290 might be very active in an ID

NOTE Confidence: 0.800555637777778

00:05:47.290 --> 00:05:49.117 file type tumor in an IDH mutant

NOTE Confidence: 0.800555637777778

00:05:49.182 --> 00:05:51.030 paradigm actually is shifted.

NOTE Confidence: 0.800555637777778

00:05:51.030 --> 00:05:52.914 Towards normal metabolism and

NOTE Confidence: 0.800555637777778

00:05:52.914 --> 00:05:53.856 oxidative phosphorylation,

NOTE Confidence: 0.800555637777778

00:05:53.860 --> 00:05:55.590 and is another mediator of

NOTE Confidence: 0.800555637777778

00:05:55.590 --> 00:05:57.320 better outcomes in these cases,

NOTE Confidence: 0.800555637777778

00:05:57.320 --> 00:05:59.511 and we have designed a study as

NOTE Confidence: 0.800555637777778

00:05:59.511 --> 00:06:02.150 part of my CI project where we

NOTE Confidence: 0.800555637777778

00:06:02.150 --> 00:06:04.180 have a prospective excuse me.

NOTE Confidence: 0.800555637777778

00:06:04.180 --> 00:06:05.952 Observational cohort 2 cohorts

NOTE Confidence: 0.800555637777778

00:06:05.952 --> 00:06:08.167 where both patients recruited both

NOTE Confidence: 0.800555637777778

00:06:08.167 --> 00:06:10.072 groups of patients recruited at

NOTE Confidence: 0.800555637777778

00:06:10.072 --> 00:06:12.172 Yale have a diagnosis of glioma.

NOTE Confidence: 0.800555637777778

00:06:12.180 --> 00:06:14.350 One group of patients has known ID

NOTE Confidence: 0.800555637777778

00:06:14.350 --> 00:06:16.554 H mutant glioma and one group of

NOTE Confidence: 0.800555637777778

00:06:16.554 --> 00:06:18.372 patients has known DH well type,

NOTE Confidence: 0.800555637777778

00:06:18.380 --> 00:06:19.880 so we'll perform for these patients.

NOTE Confidence: 0.622209846

00:06:19.880 --> 00:06:21.848 Brain MRI will measure the lactate.

NOTE Confidence: 0.622209846

00:06:21.850 --> 00:06:24.766 As I mentioned, we also can measure 2 hydroxy

NOTE Confidence: 0.622209846

00:06:24.766 --> 00:06:26.749 glutarate with protomer spectroscopy.

NOTE Confidence: 0.622209846

00:06:26.750 --> 00:06:28.970 We'll measure FDG pet. We'll perform

NOTE Confidence: 0.622209846

00:06:28.970 --> 00:06:30.450 whole genome methylation studies,

NOTE Confidence: 0.622209846

00:06:30.450 --> 00:06:33.480 and we'll measure clinical outcomes in

NOTE Confidence: 0.622209846

00:06:33.480 --> 00:06:35.500 radiography or conventional pathophysiologic

NOTE Confidence: 0.622209846

00:06:35.568 --> 00:06:37.700 outcomes through standard scanning.

NOTE Confidence: 0.622209846

00:06:37.700 --> 00:06:40.080 So I've had the privilege of actually

NOTE Confidence: 0.622209846

00:06:40.080 --> 00:06:41.370 scanning several patients now,

NOTE Confidence: 0.622209846

00:06:41.370 --> 00:06:43.010 and I can show you the way that

NOTE Confidence: 0.622209846

00:06:43.010 --> 00:06:44.110 this actually seems to work.

NOTE Confidence: 0.622209846

00:06:44.110 --> 00:06:46.470 So I H. Mutant tumor here is seen

NOTE Confidence: 0.622209846

00:06:46.470 --> 00:06:48.830 as seen in generally appears quite

NOTE Confidence: 0.622209846

00:06:48.830 --> 00:06:50.950 similar on a standard MRI.

NOTE Confidence: 0.622209846

00:06:50.950 --> 00:06:53.910 This is actually also a high grade glioma,

NOTE Confidence: 0.622209846

00:06:53.910 --> 00:06:54.990 but a main difference.

NOTE Confidence: 0.622209846

00:06:54.990 --> 00:06:56.070 This is an oligodendroglioma

NOTE Confidence: 0.622209846

00:06:56.070 --> 00:06:57.090 that's and otherwise.

NOTE Confidence: 0.622209846

00:06:57.090 --> 00:06:58.795 Characterizes anaplastic or Grade 3

NOTE Confidence: 0.622209846

00:06:58.795 --> 00:07:01.373 and so an IH mutation is present in

NOTE Confidence: 0.622209846

00:07:01.373 --> 00:07:03.683 this tumor and you can see that it

NOTE Confidence: 0.622209846

00:07:03.683 --> 00:07:05.837 actually looks quite different with the

NOTE Confidence: 0.622209846

00:07:05.837 --> 00:07:08.135 Warburg index and so this is a tumor

NOTE Confidence: 0.622209846

00:07:08.135 --> 00:07:09.684 that a seasoned neuro oncologist would

NOTE Confidence: 0.622209846

00:07:09.684 --> 00:07:11.400 know is going to behave differently.

NOTE Confidence: 0.622209846

00:07:11.400 --> 00:07:13.255 And I think that actually the metabolic

NOTE Confidence: 0.622209846

00:07:13.255 --> 00:07:14.640 image really underscores the behavior.

NOTE Confidence: 0.622209846

00:07:14.640 --> 00:07:16.620 These patients clearly do much better

NOTE Confidence: 0.622209846

00:07:16.620 --> 00:07:18.720 than patients who have glioblastomas

NOTE Confidence: 0.622209846

00:07:18.720 --> 00:07:20.016 and so another method that we've

NOTE Confidence: 0.622209846

00:07:20.016 --> 00:07:21.452 been working on which was also

NOTE Confidence: 0.622209846

00:07:21.452 --> 00:07:22.516 introduced by Doctor Constable,

NOTE Confidence: 0.622209846

00:07:22.520 --> 00:07:23.712 is deuterium metabolic imaging,

NOTE Confidence: 0.622209846

00:07:23.712 --> 00:07:26.300 and this is a through my collaborators.

NOTE Confidence: 0.622209846

00:07:26.300 --> 00:07:27.540 We use something called.

NOTE Confidence: 0.622209846

00:07:27.540 --> 00:07:28.470 Stable isotope method.

NOTE Confidence: 0.622209846

00:07:28.470 --> 00:07:29.880 So we actually give someone

NOTE Confidence: 0.622209846

00:07:29.880 --> 00:07:31.008 they just drink it,

NOTE Confidence: 0.622209846

00:07:31.010 --> 00:07:32.455 they just drink deuterated glucose

NOTE Confidence: 0.622209846

00:07:32.455 --> 00:07:33.900 and you can actually watch

NOTE Confidence: 0.622209846

00:07:33.953 --> 00:07:35.328 the tutorial and the scanner.

NOTE Confidence: 0.622209846

00:07:35.330 --> 00:07:37.178 You can watch it go through this whole

NOTE Confidence: 0.622209846

00:07:37.178 --> 00:07:38.538 paradigm that I laid out for you.

NOTE Confidence: 0.622209846

00:07:38.540 --> 00:07:40.367 It's a slight difference in that we

NOTE Confidence: 0.622209846

00:07:40.367 --> 00:07:42.226 measure glutamate and glutamine as a

NOTE Confidence: 0.622209846

00:07:42.226 --> 00:07:43.590 measure of oxidative phosphorylation,

NOTE Confidence: 0.622209846

00:07:43.590 --> 00:07:45.298 and we can't differentiate the two and

NOTE Confidence: 0.622209846

00:07:45.298 --> 00:07:47.067 you'll see it referred to as a GLX,

NOTE Confidence: 0.622209846

00:07:47.070 --> 00:07:48.792 but that's the measure of oxidative

NOTE Confidence: 0.622209846

00:07:48.792 --> 00:07:49.940 phosphorylation and to detect

NOTE Confidence: 0.622209846

00:07:49.993 --> 00:07:51.409 the Warburg effect in this case,

NOTE Confidence: 0.622209846

00:07:51.410 --> 00:07:53.468 we once again actually have direct

NOTE Confidence: 0.622209846

00:07:53.468 --> 00:07:55.637 measures of bicyclists and oxidative

16

NOTE Confidence: 0.622209846

00:07:55.637 --> 00:07:56.369 phosphorylation.

NOTE Confidence: 0.622209846

00:07:56.370 --> 00:07:58.026 This is the technique that was

NOTE Confidence: 0.622209846

00:07:58.026 --> 00:07:58.578 also developed.

NOTE Confidence: 0.622209846

00:07:58.580 --> 00:08:01.310 At Gill and I'm excited to show

NOTE Confidence: 0.622209846

00:08:01.310 --> 00:08:04.106 you some more data from HDMI so

NOTE Confidence: 0.622209846

00:08:04.106 --> 00:08:05.736 the Warburg effect is seen.

NOTE Confidence: 0.622209846

00:08:05.740 --> 00:08:07.660 Here we saw before as well.

NOTE Confidence: 0.622209846

00:08:07.660 --> 00:08:08.752 This is another patient.

NOTE Confidence: 0.622209846

00:08:08.752 --> 00:08:10.784 This is my patient who had glioblastoma

NOTE Confidence: 0.622209846

00:08:10.784 --> 00:08:13.143 and you can see lactate is far

NOTE Confidence: 0.622209846

00:08:13.143 --> 00:08:14.573 exceeding glutamate and glutamine

NOTE Confidence: 0.622209846

00:08:14.573 --> 00:08:16.313 and really highlights the metabolic

NOTE Confidence: 0.622209846

00:08:16.313 --> 00:08:18.620 activity of the tumor and we actually

NOTE Confidence: 0.622209846

00:08:18.620 --> 00:08:20.510 have been able to image multiple

NOTE Confidence: 0.622209846

00:08:20.569 --> 00:08:22.277 patients with glioblastomas at

NOTE Confidence: 0.622209846

00:08:22.277 --> 00:08:24.412 different times in their treatment.

NOTE Confidence: 0.622209846

00:08:24.420 --> 00:08:25.480 So this is a patient.

NOTE Confidence: 0.622209846

00:08:25.480 --> 00:08:27.760 Also a separate patient who has

NOTE Confidence: 0.622209846

00:08:27.760 --> 00:08:29.280 an asthma at diagnosis.

NOTE Confidence: 0.622209846

00:08:29.280 --> 00:08:30.594 And I mentioned that the first

NOTE Confidence: 0.622209846

00:08:30.594 --> 00:08:32.089 stage of treatment the patients have

NOTE Confidence: 0.622209846

00:08:32.089 --> 00:08:33.534 radiation with chemotherapy and we

NOTE Confidence: 0.622209846

00:08:33.534 --> 00:08:34.877 actually weren't able to detect

NOTE Confidence: 0.622209846

00:08:34.877 --> 00:08:36.173 the Warburg effect in this case.

NOTE Confidence: 0.622209846

00:08:36.180 --> 00:08:38.091 And then you can see two instances

NOTE Confidence: 0.622209846

00:08:38.091 --> 00:08:40.197 where we were able to scan patients

NOTE Confidence: 0.622209846

00:08:40.197 --> 00:08:42.369 who had recurrent disease and we were

NOTE Confidence: 0.622209846

00:08:42.369 --> 00:08:44.206 able to detect Warburg effects that

NOTE Confidence: 0.622209846

00:08:44.206 --> 00:08:45.574 actually appear slightly different.

NOTE Confidence: 0.622209846

00:08:45.580 --> 00:08:47.939 So this this tells us that these

NOTE Confidence: 0.622209846

00:08:47.939 --> 00:08:48.613 techniques might,

NOTE Confidence: 0.622209846

00:08:48.620 --> 00:08:50.516 in addition to telling us something

NOTE Confidence: 0.622209846

00:08:50.516 --> 00:08:52.619 about diagnosis and maybe even prognosis.

NOTE Confidence: 0.622209846

00:08:52.620 --> 00:08:54.720 They may tell us about treatment

NOTE Confidence: 0.622209846

00:08:54.720 --> 00:08:56.120 of of the tumors.

NOTE Confidence: 0.622209846

00:08:56.120 --> 00:08:58.454 So I think future directions for

NOTE Confidence: 0.622209846

00:08:58.454 --> 00:09:00.010 metabolic imaging and neurology

NOTE Confidence: 0.780793345875

00:09:00.075 --> 00:09:01.899 at Yale are rich and exciting.

NOTE Confidence: 0.780793345875

00:09:01.900 --> 00:09:03.868 The Warburg index, the technique I

NOTE Confidence: 0.780793345875

00:09:03.868 --> 00:09:05.958 told you about using MRI and PET.

NOTE Confidence: 0.780793345875

00:09:05.960 --> 00:09:07.370 We're hoping to complete the

NOTE Confidence: 0.780793345875

00:09:07.370 --> 00:09:08.498 recruitment of both cohorts.

NOTE Confidence: 0.780793345875

00:09:08.500 --> 00:09:09.568 We're looking forward to

NOTE Confidence: 0.780793345875

00:09:09.568 --> 00:09:10.636 measuring these genetic radio,

NOTE Confidence: 0.780793345875

00:09:10.640 --> 00:09:12.132 graphic and clinical links.

NOTE Confidence: 0.780793345875

00:09:12.132 --> 00:09:13.997 This is a clinically available,

NOTE Confidence: 0.780793345875

00:09:14.000 --> 00:09:15.152 rapidly scalable test that

NOTE Confidence: 0.780793345875

00:09:15.152 --> 00:09:16.304 was developed at Yale.

NOTE Confidence: 0.780793345875

00:09:16.310 --> 00:09:18.347 I think this is exactly the type

NOTE Confidence: 0.780793345875

00:09:18.347 --> 00:09:20.457 of tool that Y CI is featuring,

NOTE Confidence: 0.780793345875

00:09:20.460 --> 00:09:21.805 and we're hoping to deploy

NOTE Confidence: 0.780793345875

00:09:21.805 --> 00:09:23.150 this into clinical trials in

NOTE Confidence: 0.780793345875

00:09:23.199 --> 00:09:24.589 the future and then determine

NOTE Confidence: 0.780793345875

00:09:24.589 --> 00:09:26.280 metabolic imaging is also a Gale.

NOTE Confidence: 0.780793345875

00:09:26.280 --> 00:09:27.231 Your own technique,

NOTE Confidence: 0.780793345875

00:09:27.231 --> 00:09:28.816 which we are also actually

NOTE Confidence: 0.862388878571429

00:09:29.050 --> 00:09:29.980 currently trying to

NOTE Confidence: 0.862388878571429

00:09:29.980 --> 00:09:31.220 deploy to clinical trials,

NOTE Confidence: 0.7950002775

00:09:31.350 --> 00:09:32.802 and also we're looking forward to

NOTE Confidence: 0.7950002775

00:09:32.802 --> 00:09:34.609 deploying this on our clinical scanners.

NOTE Confidence: 0.7950002775

00:09:34.610 --> 00:09:37.774 Perhaps first at Yale, New Haven Hospital.

NOTE Confidence: 0.7950002775

00:09:37.780 --> 00:09:39.404 I think that these will tell us

NOTE Confidence: 0.7950002775

00:09:39.404 --> 00:09:40.600 as always mentioning diagnosis,

NOTE Confidence: 0.7950002775

00:09:40.600 --> 00:09:42.460 prognosis but also measures of

NOTE Confidence: 0.7950002775

00:09:42.460 --> 00:09:44.320 treatment effect in the future.

NOTE Confidence: 0.7950002775

00:09:44.320 --> 00:09:46.476 And so I want to thank everyone

NOTE Confidence: 0.7950002775

00:09:46.476 --> 00:09:48.320 who's helped me get this far.

NOTE Confidence: 0.7950002775

00:09:48.320 --> 00:09:50.456 This is my lab, my postgraduate,

NOTE Confidence: 0.7950002775

00:09:50.460 --> 00:09:51.800 the alumni of my lab.

NOTE Confidence: 0.7950002775

00:09:51.800 --> 00:09:53.546 Of course the YC Scholar Award

NOTE Confidence: 0.7950002775

00:09:53.546 --> 00:09:55.628 and the privilege to be here and

NOTE Confidence: 0.7950002775

00:09:55.628 --> 00:09:57.053 also my collaborators are O.

NOTE Confidence: 0.7950002775

00:09:57.060 --> 00:09:58.252 One for deterring metabolic

NOTE Confidence: 0.7950002775

00:09:58.252 --> 00:10:00.757 energy and I want to I would be

NOTE Confidence: 0.7950002775

00:10:00.757 --> 00:10:02.377 remiss to not thank everyone,

NOTE Confidence: 0.7950002775

00:10:02.380 --> 00:10:03.612 but especially the teams.

NOTE Confidence: 0.7950002775

00:10:03.612 --> 00:10:05.859 Actually my first TL one award was

NOTE Confidence: 0.7950002775

00:10:05.859 --> 00:10:07.887 with the Stanford spectrum with Doctor.

NOTE Confidence: 0.7950002775

00:10:07.890 --> 00:10:09.898 Steinberg, but in addition,

NOTE Confidence: 0.7950002775

00:10:09.898 --> 00:10:12.408 my my mentor doctor Rect

NOTE Confidence: 0.7950002775

00:10:12.408 --> 00:10:14.720 Stanford doctors hafler amoro,

NOTE Confidence: 0.7950002775

00:10:14.720 --> 00:10:16.922 bearing Blonden and Kim and our

NOTE Confidence: 0.7950002775

00:10:16.922 --> 00:10:19.499 fellow Mary Barton at Yale Neurology,

NOTE Confidence: 0.7950002775

00:10:19.500 --> 00:10:21.084 doctors Channel and Moliterno.

NOTE Confidence: 0.7950002775

00:10:21.084 --> 00:10:21.876 Yale neurosurgery.

NOTE Confidence: 0.7950002775

00:10:21.880 --> 00:10:23.752 Of course, the YCI,

NOTE Confidence: 0.7950002775

00:10:23.752 --> 00:10:26.092 including Doctor Shapiro Cantley and

NOTE Confidence: 0.7950002775

00:10:26.092 --> 00:10:28.979 Sinha of course MRC that's my buzzer.

NOTE Confidence: 0.7950002775

00:10:28.980 --> 00:10:31.680 I'm overtime, but I'm almost done,

NOTE Confidence: 0.7950002775

00:10:31.680 --> 00:10:33.856 doctors, Rothman, doctors, Degraff,

NOTE Confidence: 0.7950002775

00:10:33.856 --> 00:10:35.960 Dr, Defeater, and then of course,

NOTE Confidence: 0.7950002775

00:10:35.960 --> 00:10:37.000 at the Yellow Pet Center.

NOTE Confidence: 0.7950002775

00:10:37.000 --> 00:10:37.728 Doctors Carson.

NOTE Confidence: 0.7950002775

00:10:37.728 --> 00:10:39.548 And Chen and the last,

NOTE Confidence: 0.7950002775

00:10:39.550 --> 00:10:40.622 but definitely not least,

NOTE Confidence: 0.7950002775

00:10:40.622 --> 00:10:40.890 doctors,

NOTE Confidence: 0.7950002775

00:10:40.890 --> 00:10:42.390 Contessa and Bindra with Yale

NOTE Confidence: 0.7950002775

00:10:42.390 --> 00:10:42.990 Radiation Oncology.

NOTE Confidence: 0.7950002775

00:10:42.990 --> 00:10:44.620 So thank you guys very much for your time.