WEBVTT

1 00:00:00.000 --> 00:00:06.959 Hello and welcome to an introduction video about the Deuterium Metabolic imaging or dmi.

2 00:00:06.959 --> 00:00:12.300 In this video we'll try to explain what the Deuterium Metabolic imaging is.

3 00:00:12.300 --> 00:00:19.640 And to answer that we should know what the theorem is and what metabolic imaging is.

4 00:00:19.640 --> 00:00:25.280 For more would like to explain why you want to use the Deuterium Metabolic imaging or dmi.

5 00:00:25.280 --> 00:00:33.868 What do you need to run DMI at your particular site and where can you find the methods and other materials at this website,

6 00:00:33.868 --> 00:00:39.240 so that you can actually run dmi agile at your side.

7 00:00:39.240 --> 00:00:52.906 First, what is dmi? Dmi is part of a large family of isotope labeling and tracing methods that include carbon 13 amorous hyperpolarized Emerson Emirates.

8 00:00:52.906 --> 00:00:59.340 I nitrogen 15. Amorous oxygen 17 amorous and as a few more as well.

9 00:00:59.340 --> 00:01:04.081 All of these methods, they are aimed at detecting dynamic better.

10 00:01:04.081 --> 00:01:13.030 Poly part ways by following the fate of the Isotope from a given substrate into a variety of metabolic products.

11 00:01:13.030 --> 00:01:14.918 Let's look at an example.

12 00:01:14.918 --> 00:01:20.441 Let's look at glucose, which is a very important substrate for for example,

13 00:01:20.441 --> 00:01:30.540 brain metabolism to glucose is being taken up by the brain and undergoes glycolysis and being converted among many other things into lactic.

14 00:01:30.540 --> 00:01:36.849 Update can enter the TVA cycle where ultimately it can be converted to glutamate.

15 00:01:36.849 --> 00:01:38.225 Now, what we can do,

16 00:01:38.225 --> 00:01:43.596 we can measure the glutamate and elected and glucose to lactate in the glutamate.

17 00:01:43.596 --> 00:01:45.495 If we mention them overtime.

18 00:01:45.495 --> 00:01:47.722 We get horizontal lines because.

19 00:01:47.722 --> 00:01:51.653 The glutamate concentration doesn't really change overtime.

20 00:01:51.653 --> 00:01:54.862 The lactate concentration doesn't really change.

21 00:01:54.862 --> 00:01:59.578 Overtime and that is because the system is in a metabolic steady state.

22 00:01:59.578 --> 00:02:06.980 The elected concentration doesn't change because the number of molecules of like their monitors are being formed.

23 00:02:06.980 --> 00:02:13.310 Is equal to the number of molecules that are being broken down so therefore the in minus out is 0?

24 00:02:13.310 --> 00:02:18.576 Show measuring just the total pool as she would do with Protel Emirates.

25 00:02:18.576 --> 00:02:27.960 For example, doesn't give you any information on how fast this part way is that where isotope labeling strategies come in.

26 00:02:27.960 --> 00:02:38.197 If we now use glucose but it has now been isotopically labeled in the one position year or in the 6 position or in both positions at the same time

27 00:02:38.197 --> 00:02:42.723 that she 13 labeled glucose still undergoes the same metabolism.

28 00:02:42.723 --> 00:02:54.144 Where these are converted to lactate in which now the sea turtle labels in the 3 position like that can enter the Tissier cycle and ultimately that carbon 30 label

29 00:02:54.144 --> 00:02:58.669 is ending up in the four position of roommate now the appearance.

30 00:02:58.669 --> 00:03:03.098 Of the carbon Tutti label can be followed overtime for example,

31 00:03:03.098 --> 00:03:10.502 with carbon 13 NMR and then you can see the build up of the elected here in the build up of the glutamate.

32 00:03:10.502 --> 00:03:13.132 Now the system is still in metabolic.

33 00:03:13.132 --> 00:03:15.347 Steady state elected pool size.

34 00:03:15.347 --> 00:03:19.360 The total amount of lactate being present doesn't change.

35 00:03:19.360 --> 00:03:22.473 However, the system is not in a nicer topic.

36 00:03:22.473 --> 00:03:25.795 Steady state yet in the beginning of the curve,

37 00:03:25.795 --> 00:03:29.740 there is more seat urchin labeled like that being formed.

38 00:03:29.740 --> 00:03:36.064 Denary broken down and you can see the amount or she turtle level like that being built up.

39 00:03:36.064 --> 00:03:39.365 Now by measuring these kind of turnover curves.

40 00:03:39.365 --> 00:03:51.199 You can determine how fast is metabolic pathway is Furthermore simply the presence of C13 elected already proved that this part way is metabolically active.

41 00:03:51.199 --> 00:03:57.659 Now these curves can be measured as a concentration of the C 13.

42 00:03:57.659 --> 00:04:03.268 Fable metabolite overtime, but you can also convert it into a fractional enrichment,

43 00:04:03.268 --> 00:04:06.104 which is basically given by this equation.

44 00:04:06.104 --> 00:04:12.900 The amount of carbon 13 labeled Metabolite divided by the total pool size of the metabolite times 100%

45 00:04:12.900 --> 00:04:17.254 and then this curve is being converted into these kind of curves.

46 00:04:17.254 --> 00:04:22.531 Now you can see that from all the glucose that is present in a tissue about 80%

47 00:04:22.531 --> 00:04:28.870 is carbon 13 labeled from all the glutamate after about an hour and a half present in a tissue.

48 00:04:28.870 --> 00:04:31.750 About 40% is carbon 13 labeled.

49 00:04:31.750 --> 00:04:36.680 Now from these kind of curves you can measure these kind of curves two ways.

50 00:04:36.680 --> 00:04:40.024 One way is dynamically where you measure data point.

51 00:04:40.024 --> 00:04:45.702 Let's say every five or every 10 minutes and from then the turnover of these metabolites.

52 00:04:45.702 --> 00:04:49.298 You can get absolute metabolic fluxes in absolute units.

53 00:04:49.298 --> 00:04:59.584 Micromort program per minute. Sometimes is not necessary or practical in that case you can also do a steady state measurement where you only mention one data set.

54 00:04:59.584 --> 00:05:08.779 Let's say between these 2 lines about an hour and a half after you start the infusion that is circled steady state metabolic imaging experiment.

55 00:05:08.779 --> 00:05:13.115 And this proves the presence of metabolic pathway activity.

56 00:05:13.115 --> 00:05:16.439 If you see again see 30 lactate being formed.

57 00:05:16.439 --> 00:05:21.199 Then this part way must be present an must be active.

58 00:05:21.199 --> 00:05:24.745 Now these kind of experiments have been done for decades,

59 00:05:24.745 --> 00:05:27.557 carbon 13 NMR as being the classical example.

60 00:05:27.557 --> 00:05:36.298 Here is a typical C 13 volume in the occipital cortex of the human brain and it is a spectrum that you get from that volume with carbon 13 NMR

61 00:05:36.298 --> 00:05:46.994 and you can indeed see that the security level glucose has been converted to glutamate into glutamine and to lactate and that will provide you the information about this part

62 00:05:46.994 --> 00:05:58.384 ways. The downside of carbon to Tina Marie's it has a fairly low sensitivity that translate into large volumes and therefore the imaging is typically not really viable.

63 00:05:58.384 --> 00:06:02.339 It's typically see 30 metabolic spectroscopy.

64 00:06:02.339 --> 00:06:04.470 It is technically also very demanding.

65 00:06:04.470 --> 00:06:06.872 You need to have good spatial organization.

66 00:06:06.872 --> 00:06:16.865 You need to have polarization transfer to enhance the sensitivity need their broadband decoupling so technically this is not an easy experiment and therefore even though it is a very

67 00:06:16.865 --> 00:06:21.370 powerful research tool, it is not really a viable clinical tool.

68 00:06:21.370 --> 00:06:25.396 OK, so if we accept that carbon 13 is very powerful.

69 00:06:25.396 --> 00:06:27.826 But it's not clinically viable.

70 00:06:27.826 --> 00:06:39.069 What other options. Do we have well if you look at the glucose molecule the formulas basically C6H12O six so if the carbon 2 teen is not an option,

71 00:06:39.069 --> 00:06:44.235 then we only have the hydrogen or the oxygen to isotopically label.

72 00:06:44.235 --> 00:06:50.839 Now you could label. The oxygen ocean 17 has nuclear spin so that is possible.

73 00:06:50.839 --> 00:07:00.670 However, the label tends to rapidly exchange with water and you don't retain label long enough to map out entire metabolic pathways.

74 00:07:00.670 --> 00:07:04.060 So that leaves us with the hydrogen isotope.

75 00:07:04.060 --> 00:07:05.968 While hydrogen has 3 isotopes,

76 00:07:05.968 --> 00:07:07.629 it has the Protel Isotope,

77 00:07:07.629 --> 00:07:11.259 which we're all familiar with it has to deuterium isotope,

78 00:07:11.259 --> 00:07:15.259 which is basically an additional neutron and there is attrition,

79 00:07:15.259 --> 00:07:17.228 which has 2 additional neutral.

80 00:07:17.228 --> 00:07:19.627 The Proton and Ethereum are as stable.

81 00:07:19.627 --> 00:07:26.370 The tritium is not radioactive radioactive and therefore we will not talk about those.

82 00:07:26.370 --> 00:07:31.279 Protein is called highly abundant and deuterium makes up the rest.

83 00:07:31.279 --> 00:07:39.141 All three of them, actually have nuclear spin deuterium has a nucleus spin of one the frequency of deuterium is about 6,

84 00:07:39.141 --> 00:07:42.160 1/2 times lower than that of Proton.

85 00:07:42.160 --> 00:07:47.550 And, of course, we are very familiar with proton with hydrogen Proton.

86 00:07:47.550 --> 00:07:51.041 Isotope becauses used for MRI and use for 90%

87 00:07:51.041 --> 00:07:54.002 of all NMR an amorous in vivo as well.

88 00:07:54.002 --> 00:07:57.875 The theorem is also being used quite a lot in NMR,

89 00:07:57.875 --> 00:08:04.970 but mostly for solvents and to provide a lock signal for high resolution NMR.

90 00:08:04.970 --> 00:08:10.810 But it actually turns out that deuterium Panama in vivo is actually also very promising,

91 00:08:10.810 --> 00:08:18.882 and that is the foundation of deuterium at the public image in so if we acquire deuterium spectrum from red brain in Vivo.

92 00:08:18.882 --> 00:08:21.901 We're getting a spectrum something like this.

93 00:08:21.901 --> 00:08:23.870 It has only one signal in it,

94 00:08:23.870 --> 00:08:32.259 which is the natural abundance voter signal at correspond to about 10 min imonar word of the theory AM.

95 00:08:32.259 --> 00:08:33.556 And they should of course,

96 00:08:33.556 --> 00:08:34.755 also be lipids in there,

97 00:08:34.755 --> 00:08:40.139 but lipids are in the signal to noise typically not high enough for lipids are very low.

98 00:08:40.139 --> 00:08:42.677 If you want to summarize the spectrum like this.

99 00:08:42.677 --> 00:08:51.899 It actually has really good signal to noise because the spectrum is acquired in one minute only and the secret noises high becaused deuterium has a large magnetic moment because

100 00:08:51.899 --> 00:08:55.049 of the spin. One it has short T1 relaxation times.

101 00:08:55.049 --> 00:09:02.965 It has a decent detour relaxation time so you have good sharp relatively sharp peaks and it is also a very robust method.

102 00:09:02.965 --> 00:09:05.105 You do have a nice water signal,

103 00:09:05.105 --> 00:09:08.739 which functions as an internal concentration reference?

104 00:09:08.739 --> 00:09:18.989 Which is really nice. But it is low enough so he don't need water suppression lipids are also low enough that sometimes you can detect a small little signal,

105 00:09:18.989 --> 00:09:21.519 but you don't need Liberty oppression,

106 00:09:21.519 --> 00:09:26.450 so overall. The acquisition methods can be very simple no water suppression.

107 00:09:26.450 --> 00:09:31.081 No liver suppression and finally be cause of the low larmore frequency,

108 00:09:31.081 --> 00:09:35.328 you are relatively insensitive to magnetic field and homogeneity.

109 00:09:35.328 --> 00:09:40.732 So this makes it very nice sensitive an robust method to acquire deuterium Spectra,

110 00:09:40.732 --> 00:09:42.860 an image is in Vivo.

111 00:09:42.860 --> 00:09:45.938 Now, if you now administer duty rated glucose,

112 00:09:45.938 --> 00:09:49.936 which is now has 2 deuterons at the 6 position and you wait.

113 00:09:49.936 --> 00:09:51.769 Let's say 60 minutes. Then,

114 00:09:51.769 --> 00:09:57.011 after 60 minutes. You can actually see the metabolic products of their glucose,

115 00:09:57.011 --> 00:10:07.231 which is shown here. It is basically broken down to lactate via glycolysis and that is an entry in TH cycle and it is ultimately ending up in the glutamate

116 00:10:07.231 --> 00:10:11.900 glutamine metabolic pool. Now. This again,

117 00:10:11.900 --> 00:10:14.869 the spectrum is is quite an only one minute,

118 00:10:14.869 --> 00:10:17.770 so if you have such a good signal to noise.

119 00:10:17.770 --> 00:10:24.365 You can use that signal to noise to either go really fast in time and acquire Spectra every second,

120 00:10:24.365 --> 00:10:28.322 few seconds or you can go in imaging mode and get spectrum.

121 00:10:28.322 --> 00:10:38.740 Small volumes and that's what dmi is all about so this is the setup deuterium coil in yellow Anna Proton Coil for anatomical imaging an shaming.

122 00:10:38.740 --> 00:10:42.912 And then basically the sequence is that you just acquire a 3 dimensional.

123 00:10:42.912 --> 00:10:45.110 Mr spectroscopic imaging of deuterium.

124 00:10:45.110 --> 00:10:53.962 You're going to get a TV and spectrum of all of these locations within the sensitive volume of the deuterium coil and you can see in anatomical image in the

125 00:10:53.962 --> 00:10:56.460 background that this is red brain.

126 00:10:56.460 --> 00:11:01.149 And it has an implant at humor in the white area here.

127 00:11:01.149 --> 00:11:04.822 So if you look at Spectra for the normal brain tissue.

128 00:11:04.822 --> 00:11:08.961 You have again. The glucose the glue made an elected is very,

129 00:11:08.961 --> 00:11:10.697 very low if you now look.

130 00:11:10.697 --> 00:11:12.366 A spectrum in the tumor.

131 00:11:12.366 --> 00:11:16.373 You can see that the glucose has been reduced a little bit.

132 00:11:16.373 --> 00:11:27.070 The glutamate is essentially gone and the lactate is a high and elevated so this gives us a really nice image contrast based on Mataba Lism.

133 00:11:27.070 --> 00:11:35.251 Now you can also make Maps out of out of that day that you can get a glucose map glutamate mapping elected map like that.

134 00:11:35.251 --> 00:11:40.549 Being high glutamate being low can also make a ratio map gives you really high.

135 00:11:40.549 --> 00:11:43.441 Your contrast to noise based on metabolism,

136 00:11:43.441 --> 00:11:45.740 so that's very different from MRI,

137 00:11:45.740 --> 00:11:48.631 which is always water based image contrast.

138 00:11:48.631 --> 00:11:51.654 This is now metabolism. Based image contrast.

139 00:11:51.654 --> 00:12:02.038 This can also be done on humans and ultimately it will be our hope that if there's a patient and patients coming in getting the standard battery of Clinical.

140 00:12:02.038 --> 00:12:03.876 Mr images T2 weighted flat.

141 00:12:03.876 --> 00:12:10.580 Even with a contrast and hands susceptibility weighted imaging and diffusion weighted imaging and and.

142 00:12:10.580 --> 00:12:15.529 In the same session, the shop vac will also get a deuterium metabolic image.

143 00:12:15.529 --> 00:12:17.369 And you can for example,

144 00:12:17.369 --> 00:12:25.976 generates lactate over glutamate Maps and showing you very high contrast and will provide you a different dimension.

145 00:12:25.976 --> 00:12:34.970 Metabolic dimension that has been lacking Indiana in so many studies where that I've only used MRI.

146 00:12:34.970 --> 00:12:37.845 OK so assuming that you want to use dmi?

147 00:12:37.845 --> 00:12:41.789 What do you need well you need a sequel?

148 00:12:41.789 --> 00:12:45.351 You need an RF coil and shave a squirrel or for humans.

149 00:12:45.351 --> 00:12:47.260 It might be more volume coil.

150 00:12:47.260 --> 00:12:50.250 You need in substrate administration protocol,

151 00:12:50.250 --> 00:13:00.493 which in humans could potentially just be a simple drinking of the substrate now on the next few slides will go over these items that can all be downloaded from

152 00:13:00.493 --> 00:13:03.470 the website if you know where to look.

153 00:13:03.470 --> 00:13:05.519 So the sequence.

154 00:13:05.519 --> 00:13:10.206 It suppose acquire sequence with a phase encoding blip on all 3 axis.

155 00:13:10.206 --> 00:13:17.236 There's 2 modes in which you can sample all of K space or you can sample a spherical portion of K space.

156 00:13:17.236 --> 00:13:26.744 Now this sequence can be downloaded if you go through the resources tab and then Emma methods at the moment you can download the broker 3D D.

157 00:13:26.744 --> 00:13:31.631 My method an protocol in the future will hope to extend it to a variant,

158 00:13:31.631 --> 00:13:36.600 Siemens and all the other clinical platforms as well.

159 00:13:36.600 --> 00:13:43.240 We also hope to over an advice and drawings and a treaty.

160 00:13:43.240 --> 00:13:47.519 Like print files for RF coil of preclinical RF coils.

161 00:13:47.519 --> 00:13:51.958 We hope to provide you with layout something like this,

162 00:13:51.958 --> 00:14:02.460 where you get a file that you can't really print to print the Holder that can be like populated with the RF coil elements.

163 00:14:02.460 --> 00:14:06.717 Will also provide with Phantoms the Phantom holders at the moment.

164 00:14:06.717 --> 00:14:10.404 We're still working on making this as smooth as possible.

165 00:14:10.404 --> 00:14:12.566 After this is under construction.

166 00:14:12.566 --> 00:14:13.964 But once it is ready,

167 00:14:13.964 --> 00:14:20.279 you can also find it under the resources steps and then on the RF coils.

168 00:14:20.279 --> 00:14:24.394 Of course, you need to administer the substrates on animals.

169 00:14:24.394 --> 00:14:27.633 They will typically be an intervenous infusion.

170 00:14:27.633 --> 00:14:38.898 So on the website. You can find protocols for the infusion protocol for glucose an for acetate that will give you a nice and stable fractional enrichment in the blood

171 00:14:38.898 --> 00:14:44.559 plasma. You can also be found under resources steps and then under protocols.

172 00:14:44.559 --> 00:14:49.356 Finally, when you acquire dmi data you will need to process it.

173 00:14:49.356 --> 00:14:54.330 We are offering a processing platform refer to Sdmi Wizard.

174 00:14:54.330 --> 00:14:59.245 It allows you to load in dmi data from all the major vendors.

175 00:14:59.245 --> 00:15:04.556 Ultimately, you can then walk through the data look at individual.

176 00:15:04.556 --> 00:15:16.049 Spectra you can also look at Spectra in a 2 dimensional grids or even make metabolic images as shown here that can an overlay within anatomical.

177 00:15:16.049 --> 00:15:24.769 MRI this software can be found again under resources and you can also find some data set as well that you can.

178 00:15:24.769 --> 00:15:28.759 Used to practice the software with.

179 00:15:28.759 --> 00:15:38.289 We ask you if you want to get this warfare or any of the other components to fill in a quick full form and basically said some basic information about

180 00:15:38.289 --> 00:15:44.601 your institution about your email and where you can use indicate which items you want for download.

181 00:15:44.601 --> 00:15:49.019 We will certainly not use this information to share with 3rd parties.

182 00:15:49.019 --> 00:15:52.806 It is we simply want to use this to build up an email list,

183 00:15:52.806 --> 00:15:59.054 so that we can contact people who are interested in dmi if there is a new release of the software,

184 00:15:59.054 --> 00:16:01.389 or if there's a workshop that is dmi.

185 00:16:01.389 --> 00:16:11.669 A related basically just interesting things I don't anticipate this email to go out more than once a year so that would certainly be in very limited capacity.

186 00:16:11.669 --> 00:16:15.042 Finally, the website also provides some education,

187 00:16:15.042 --> 00:16:19.340 they will be showing their frequency frequently asked questions.

188 00:16:19.340 --> 00:16:22.051 There will be some videos at the moment?

189 00:16:22.051 --> 00:16:23.903 Is there's one other video,

190 00:16:23.903 --> 00:16:34.746 but that will definitely be built up overtime will also keep an active list of ALDI my related references both from Yuan from other institutions so that you have a

191 00:16:34.746 --> 00:16:39.159 nice one place to go to download everything dmi related.

192 00:16:39.159 --> 00:16:41.354 OK, This Is This is all we wanted to say.

193 00:16:41.354 --> 00:16:43.390 In this introduction video. Of course,

194 00:16:43.390 --> 00:16:44.957 please contact. A contact us.

195 00:16:44.957 --> 00:16:48.309 If you have any questions or if you need any help.

196 00:16:48.309 --> 00:16:52.907 And we wish you the best of luck with EMI.