Grant agreement no. 667510

GLINT

Research and Innovation Action
H2020-PHC-2015-two-stage

D7.8 Ethics for scanning children and scanning of first paediatric lymphoma patient

Work Package:	7
Due date of deliverable:	31/12/2017
Actual submission date:	January 2, 2018
Lead beneficiary:	UCL
Contributors:	UCL
Reviewers:	

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Project co-funded by the European Commission within the H2020 Programme (2014-2020)		
Dissemination Level		
PU	Public	YES
CO	Confidential, only for members of the consortium (including the Commission Services)	
CI	Classified, as referred to in Commission Decision 2001/844/EC	

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Contents

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1 Version log

Version	Date	Released by	Nature of Change
V1.0	14/12/2017	Mina Kim	First version
V1.1	19/12/2017	Mina Kim	Revised

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2 Definition and acronyms

Acronyms	Definitions
T2w-mDixon	T2 weighted-modified Dixon
glucoCEST	Glucose Chemical exchange saturation transfer
MTR_{asym}	Asymmetric Magnetization Transfer Ratio

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3 Introduction

3.1 Position of D7.8 in the project

In order to assess a feasibility of commencing D7.8, it is essential to evaluate the results which have been carried out until now. So far, five adult patients have been scanned whereas data from two patients were discarded due to technical errors. Therefore, only data from three patients (patient 3,4 and 5) will be considered in this report. The technical part of experimental procedures is as follows:

- Baseline blood glucose measurements ensured that fasting blood glucose is less than 7 mM/l, random glucose less than 10 mM/l and the highest rise in glucose from baseline during infusion didn't exceed 10 mM/l rise.
- Anatomical localization images and CEST images were acquired once the glucose infusion commenced.
- 2 mins-glucose monitoring was carried out in the first 10 mins and then reduced to every 5 mins monitoring afterwards.
- The glucose infusion ran as minimal time as possible for about 30 min to 1 hour.
- The acquired CEST images were post-processed using an in-house software.

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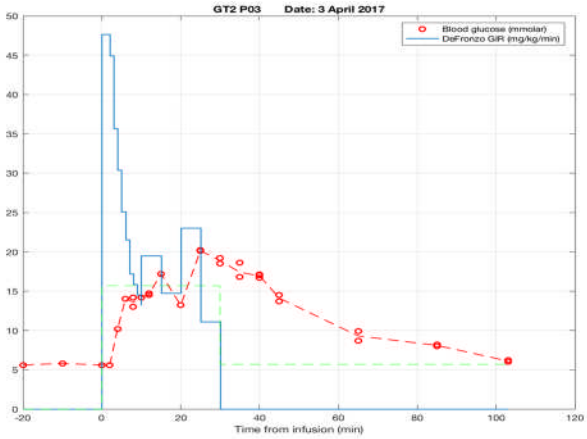
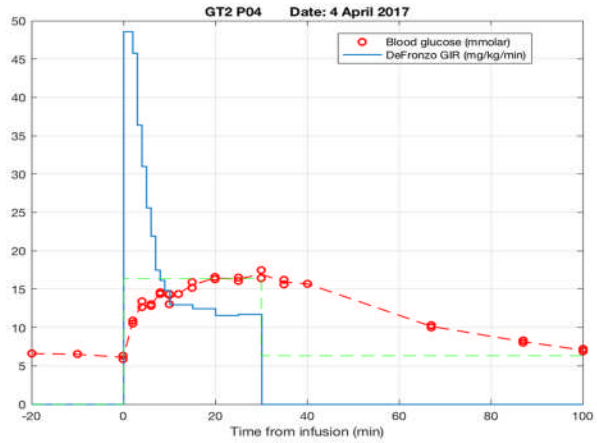
4 Report Activities carried-out and results

Hyperglycemic clamp performed using DeFronzo's algorithm [1] significantly improved control over glucose levels and minimize total infusion time.

- **Patient 3:**



- **Patient 4:**



- **Patient 5:**

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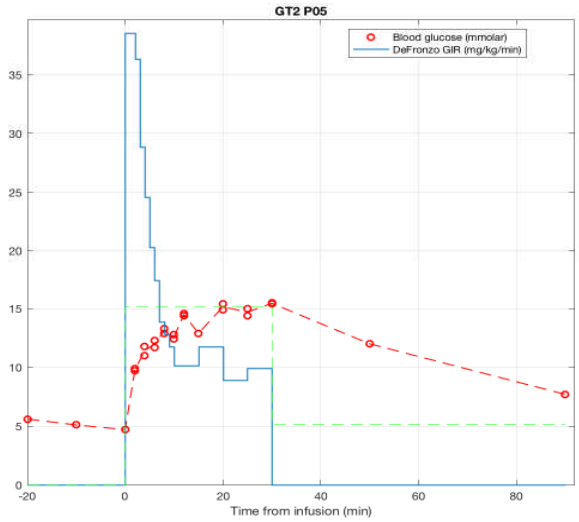
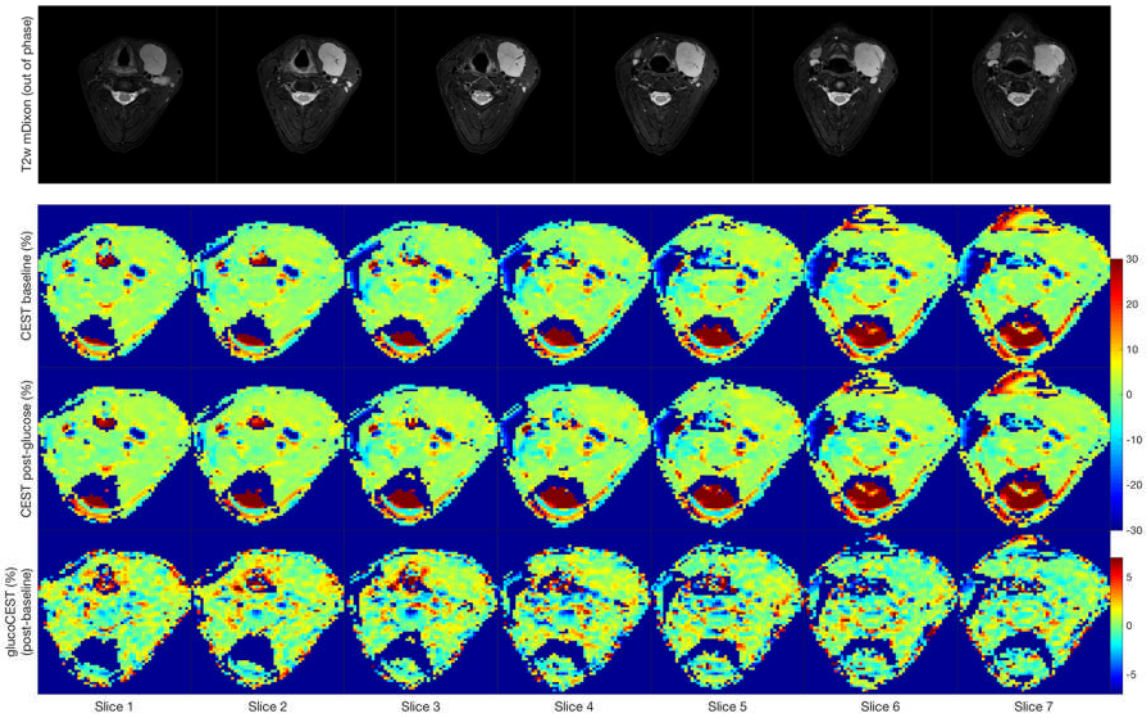


Image results of three adult lymphoma patients show no significant enhancement in CEST signal after administration of glucose infusion as displayed below.

- **Patient 3:**



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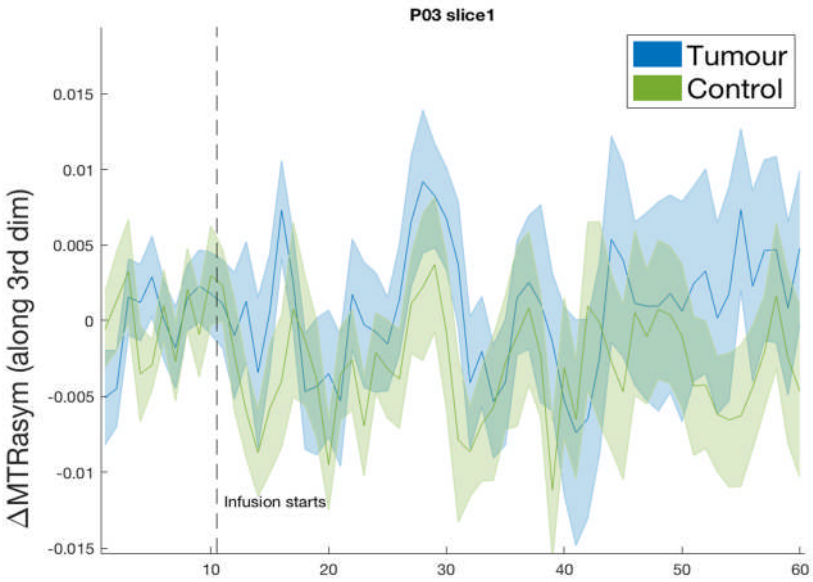

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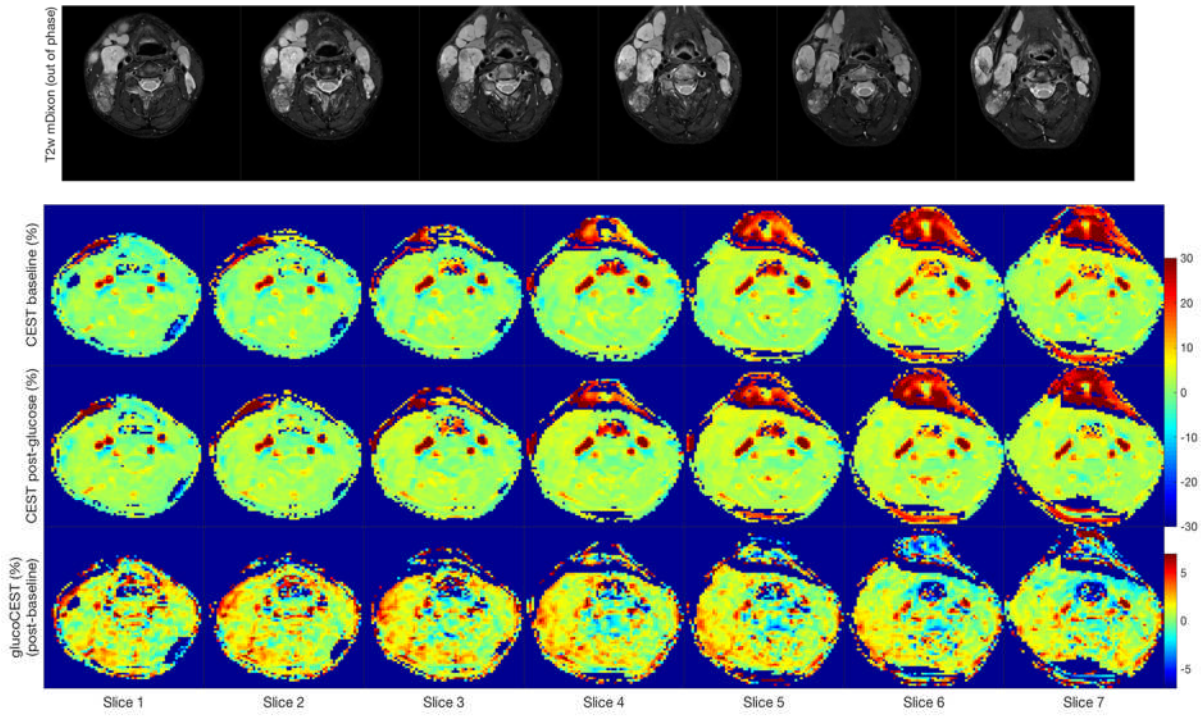
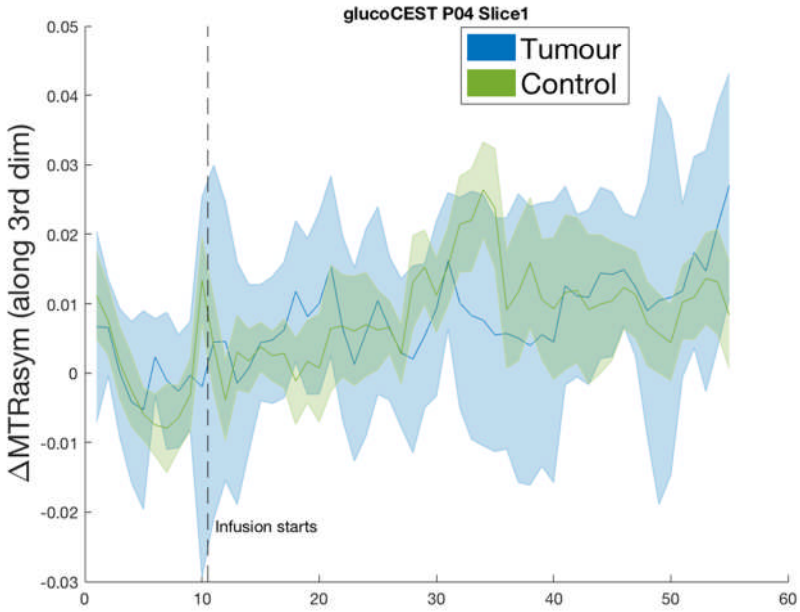
- **Patient 4:**





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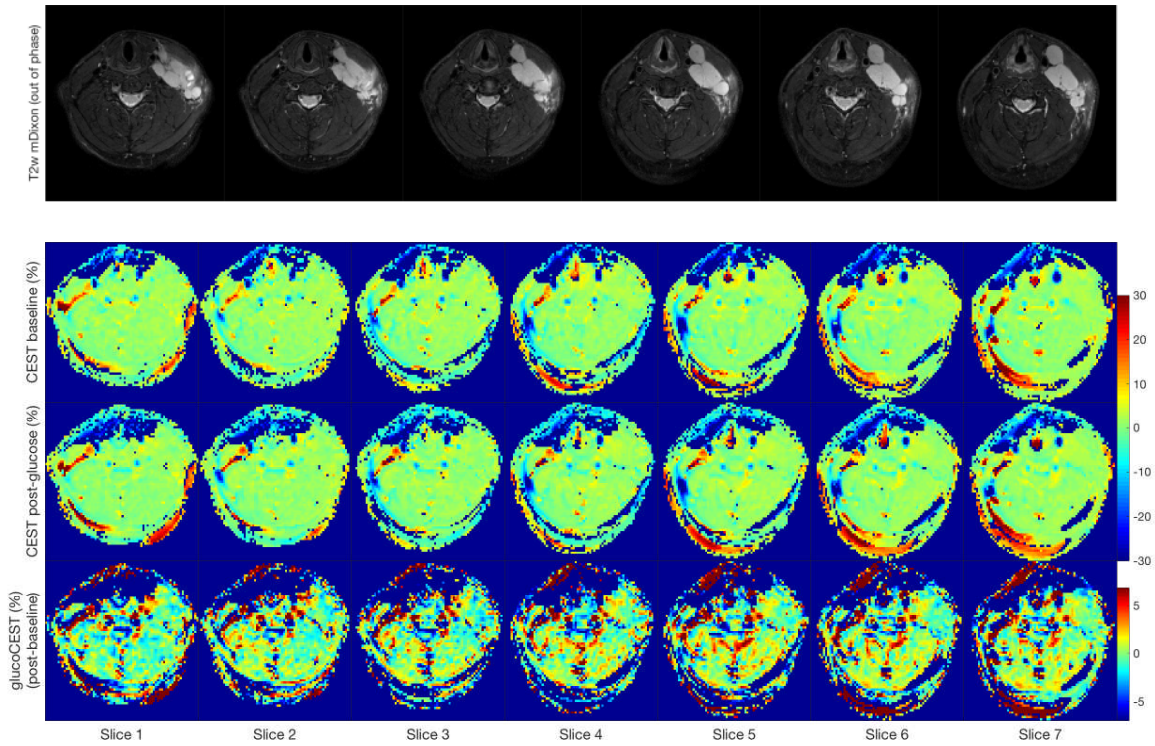
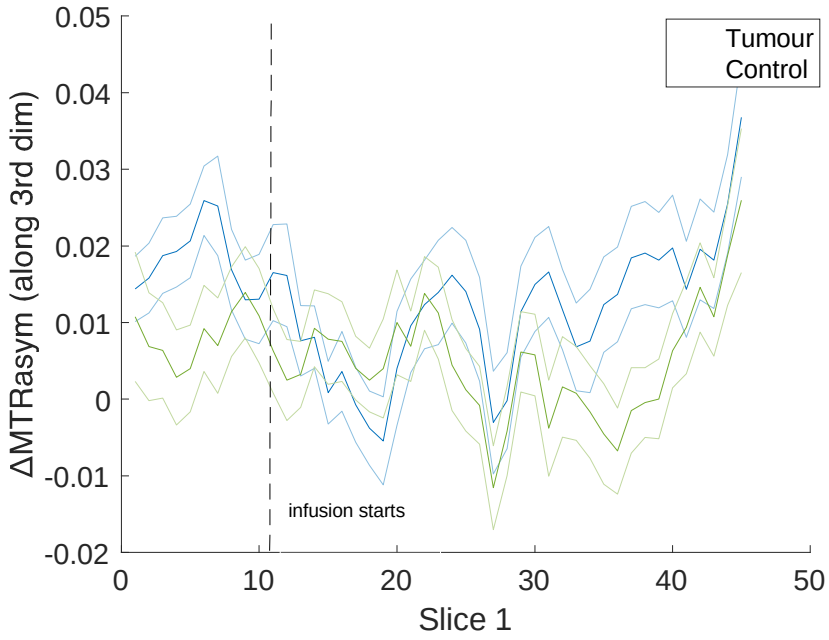
- Patient 5:





Those negative results from three adult lymphoma patients are in line with the Deliverable (D) 5.3 which was recently reported by University of Torino. As described in D5.3, the CEST contrast following natural glucose administration is dependent on several conditions such as the amount of the injected dose, the administration route and the magnetic field strength. In particular, clinical scanners (3T) as compared to high field scanner (> 3T) are

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disadvantageous for CEST detection due to the lower separation in hertz between the exchanging proton pool and the bulk water pool. In D5.3, it was demonstrated that the measured contrast in the tumour region at 3T was lower than the threshold limit of 1%, independent of glucose administration route and injected dose. A likely explanation for these results is linked to the smaller chemical shift difference between hydroxyl protons and bulk water signal at 3T (ca. 125 Hz) that results in higher direct saturation effects and reduced selectivity. As a consequence, CEST signal is less visible and limits *in vivo* detection of natural glucose. Alternative glucose analogue, such as 3-oxy-methyl-D-glucose (3OMG) is currently under investigation as a potential non-metabolisable tracer providing high GlucoCEST contrast using the same technique at 7T (see D5.2). Comparison between D-glucose and 3OMG at low field may be performed in the future upon completion of the Good Laboratory Practice (GLP)-certified 3OMG production (Work Package 6). Use of high field (7T) could also be a potential way to improve the threshold limit.

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5 Conclusions

The negative results from three adult lymphoma patients stem from low sensitivity and reduced selectivity at the field strength (3T) of a clinical scanner. We do not wish to continue further experiments using natural glucose at 3T since it is not expected to get positive results from more adult patients based on our results as well as the recent report by University of Torino. Additionally, we anticipate that UCL ethics committee will not allow further experiments due to negative results from three patients. As an alternative to natural glucose, 3-oxy-methyl-D-glucose (3OMG) is currently under investigation as a non-metabolisable glucose analogue which may provide high GlucoCEST contrast at clinical field strength. D7.8 is only partially achieved.

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Bibliography / References

[1] DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979 Sep;237(3):E214-23.

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