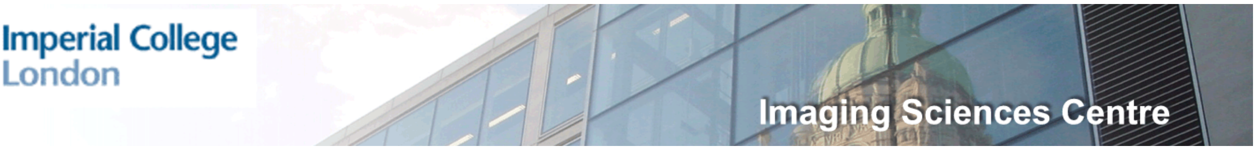

Altered adiposity after extremely preterm birth

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Introduction

• The third trimester of human development is a period of rapid adipose tissue (AT) deposition[1] .

• Infants born extremely preterm are profoundly deficient in AT, but it is possible that the pattern of adiposity may also be altered in these infants.

• It is known in children and adults that the distribution, as well as the quantity of adipose tissue (AT), is a marker of morbidity risk.

•However it is the age at which abnormal patterns of adiposity are established are not known and little is known about the deposition of ectopic fat in these infants.

Aim

To compare AT content and distribution in preterm infants at age term equivalent with term born babies and to apply ^{1}H MRS to investigate intrahepatocellular lipid (IHCL) deposition in preterm infants at the age of term.

Methods

MR Imaging

• Data were acquired from 38 infants born at < 32 weeks gestational age, at age term equivalent and 29 term-born infants.

• MRI: whole body MR images were acquired on a Phillips 1.5 Tesla system using a rapid T_1-weighted spin-echo sequence (TR 600 ms, TE 16 ms). The serial isocentre technique is employed in which infants were moved through the magnet for full body imaging. The slice and inter-slice thickness were 5 mm, requiring on average 40-50 slices per baby.

• Images were analysed using a commercially available software programme SliceOMatic, Version 4.2 (Tomovision, Montreal).

MR Spectroscopy

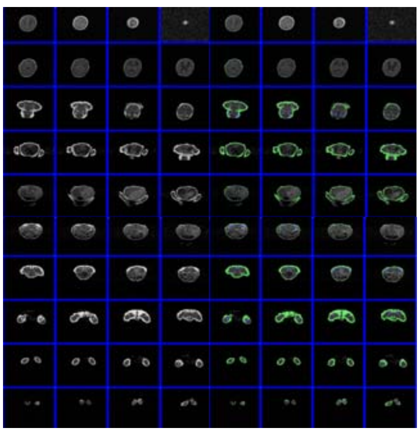
• A subset of 9 infants, 5 preterm, 4 term. IHCL data was also obtained from 7 healthy control adults, defined as BMI<25kg/m^2, age<40 years. ^{1}H MR spectra were acquired at 1.5 T from the right lobe of the liver using a PRESS sequence (TR 1500 ms/ TE 135 ms, 128 averages) without water saturation. Transverse images were used to ensure accurate positioning of the (8cm^3) voxel.

• Spectra were analysed using the AMARES algorithm included in the MRUI software package. Peak areas for all resonances were obtained and lipid resonances quantified with reference to water, after correcting for T_1 and T_2.

Results

Typical MR images from an infant before and after image segmentation are shown in figure 1. In the segmented images subcutaneous adipose tissue is coded green and internal blue.

Figure 1: ← **Whole Body MRI** ——→← **Segmented Images** →



As expected, the preterm infants-at-term were significantly lighter and shorter than the term-born infants; however there was no significant difference in head circumference standard deviation score or total percentage adiposity.

Closer examination of adipose tissue distribution showed that at term, subcutaneous AT was significantly reduced in the preterm babies term and intra-abdominal AT was increased (Table 1). There was a significant association between illness severity and increased intra-abdominal AT.

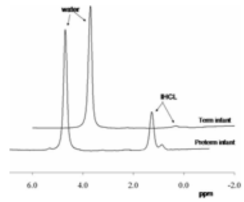
Table 1: Comparison of preterm and term born infants (means ± SD).

	Preterm (n= 38)	Term (n= 29)	Significance
Gestational age (weeks)	28.8 ± 2.1	39.9 ± 1.4	< 0.01
Birth weight (kg)	1.19 ± 0.37	3.47 ± 0.29	< 0.01
Scan weight (kg)	2.68 ± 0.61	3.24 ± 0.26	< 0.01
% Total AT	17.0 ± 4.0	18.3 ± 2.5	0.64
Subcutaneous as % of total AT	88.5 ± 2.9	91.9 ± 1.1	< 0.001
Intra-abdominal as % of total AT	4.62 ± 1.46	3.11 ± 0.63	< 0.001

Regression analysis further demonstrated that accelerated postnatal weight gain was accompanied by increased total and subcutaneous adiposity.

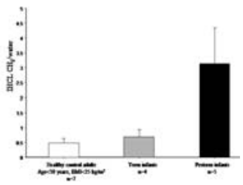
Typical ^{1}H MRS spectra obtained from the liver of a term and preterm infant are shown in Figure 2. Good quality spectra were readily obtained from all infants.

Figure 2: ^{1}H Liver Spectra from a term and preterm infant at age term-equivalent



Term infants showed similar levels of IHCL (0.69 ± 0.47) as that observed in healthy control adults (0.51 ± 0.39; p=0.91). However, preterm infants had significantly elevated levels of IHCL (3.12 ± 2.70, p<0.05) compared with both term infants (p<0.01) and healthy control adults (p<0.01), Figure 3.

Figure 3: IHCL levels in healthy control adults, term and preterm infants (at age term equivalent).



The relative increase in IHCL deposition in the preterm infants did not appear to be associated with diet or rate of postnatal weight gain. Although some of the infants did receive parenteral nutrition, breastmilk comprised 94.1 ± 0.9% of total nutrition for 4/5 preterm infants. One preterm infant received a smaller proportion of breastmilk 0.9% compared with the others, but had one of the lower levels of IHCL. No association was observed between IHCL deposition and either total or intra-abdominal adiposity.

Discussion

- Although smaller than term infants, preterm infants at term had similar total adiposity but distribution was altered[1]
- Our data provides evidence of causal pathways linking accelerated postnatal growth with increased total and subcutaneous adiposity, and illness severity with altered adipose tissue partitioning. Thus, preterm infants may be at risk of later life metabolic complications through increased and aberrant adiposity.
- Preferential deposition of adipose tissue in the abdominal compartment in preterm infants at term was observed, with reduced subcutaneous AT. Further exploration warranted to establish if this altered partitioning of adipose tissue has long term metabolic implications in this vulnerable group
- Preterm infants appear to accumulate higher levels of this ectopic fat than control term infants and adult volunteers. The clinical relevance of increased lipid in the livers of preterm infants is unclear.
- The presence of increased liver fat has been previously reported in infant malnutrition[2], however this is unlikely to be the cause in these well nourished preterm infants.
- It is possible that the increase in IHCL in preterm infants may reflect an overall alteration in the normal pattern deposition of fat, reflecting an abnormal lipid metabolism and/or adipose tissue development.

References

[1]Uthaya S et al *Pediatr Res* (2005) 57:1-6
[2]Waterlow JC *Am J Clin Nutr* (1975) 28:1330-6

Acknowledgement
We would like to thank the Medical Research Council (UK) for their financial support