Magnetisation Transfer Imaging – practical aspects

Paul Tofts

Formerly Chair of Imaging Physics, Brighton and Sussex Medical School

And Professor of Medical Physics, University College London Institute of Neurology

www.paul-tofts-phd.org

Overview

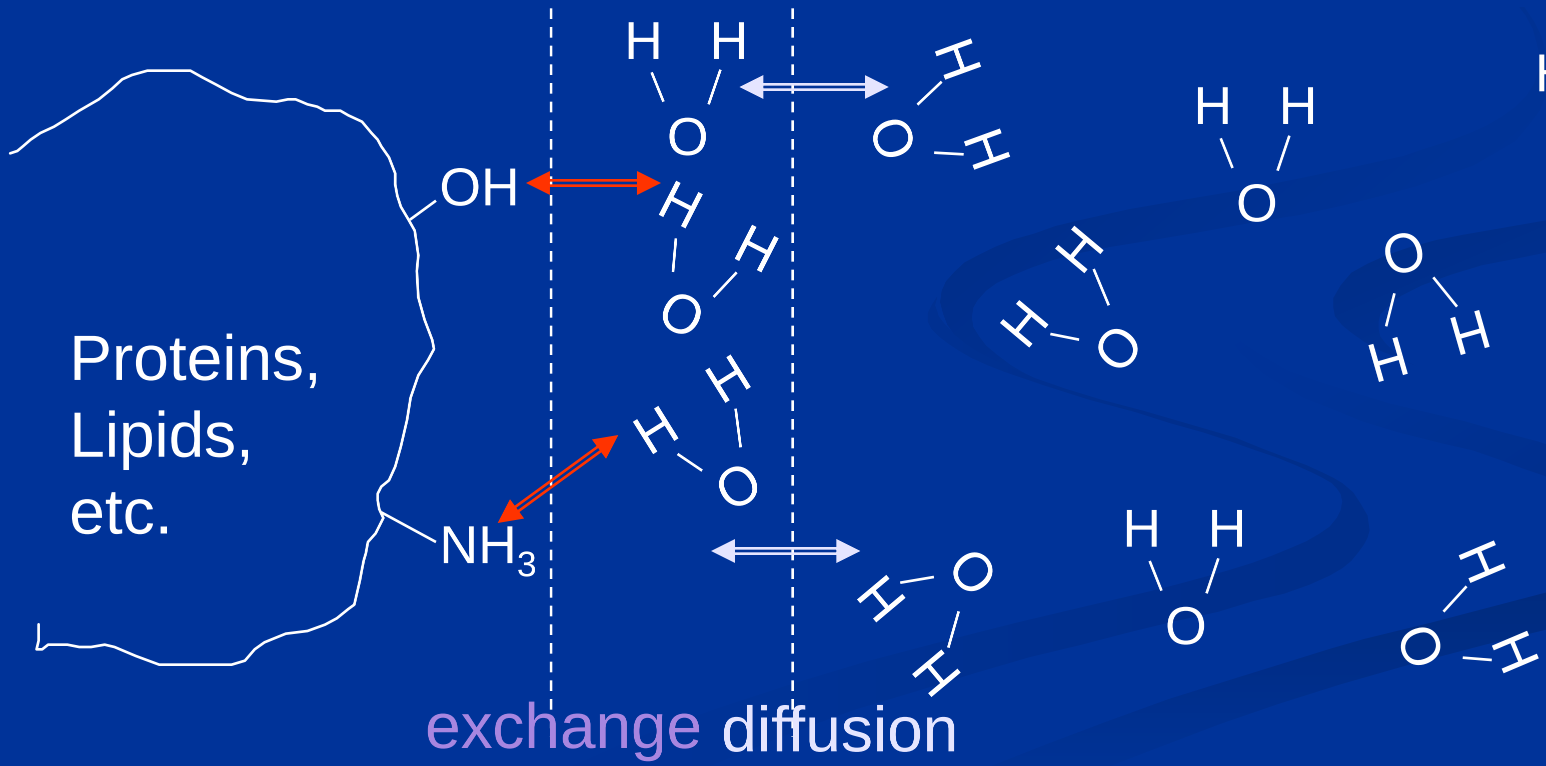
1. What is MT? The phenomenon.
2. MTR
    1. Measurement
    2. Multicentre
    3. Clinical applications
3. qMT
    1. Model
    2. Sampling schemes
    3. Clinical applications

Magnetisation Transfer

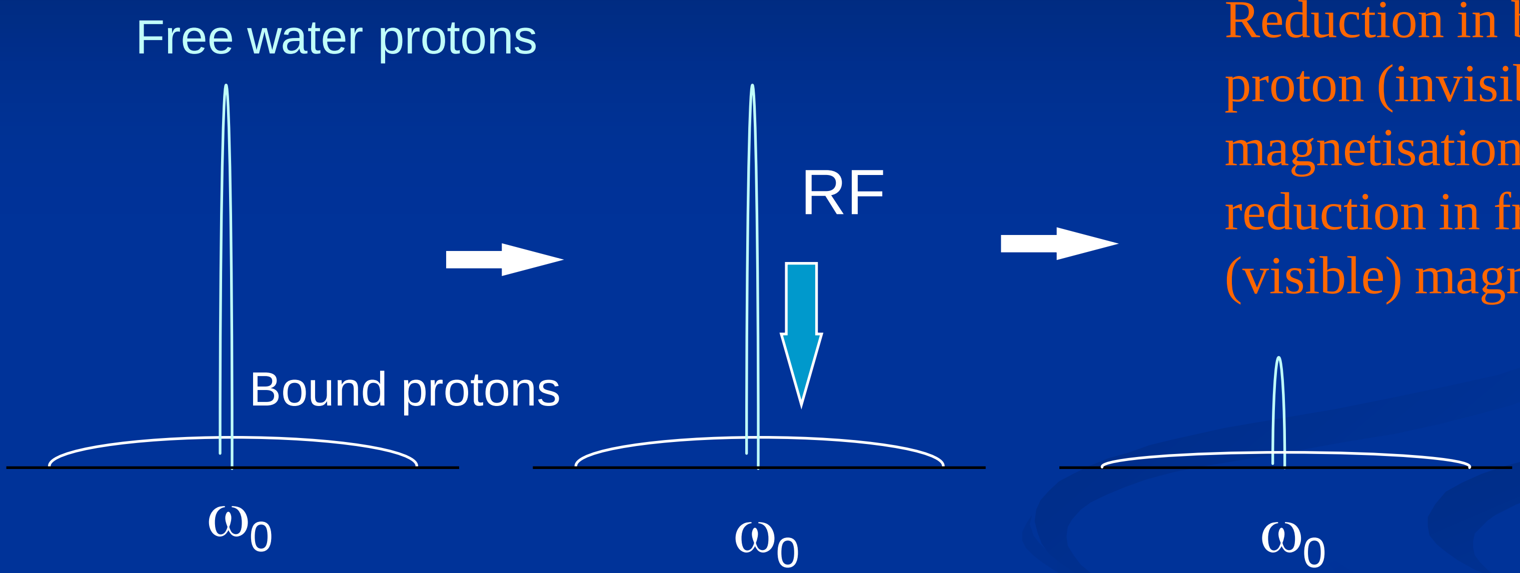
Macro molecules (invisible)
(bound protons - short T_2)

Surface

Bulk water (visible)
(free protons- long T_2)



Magnetisation Transfer - 2



Reduction in bound proton (invisible) magnetisation causes reduction in free proton (visible) magnetisation

Unsaturated - S_u

Saturated - S_s

Magnetisation Transfer Ratio

Percentage reduction in signal caused by saturating the bound pool: **units pu = percent units**

$$MTR = \frac{100.(S_u - S_s)}{S_u}$$

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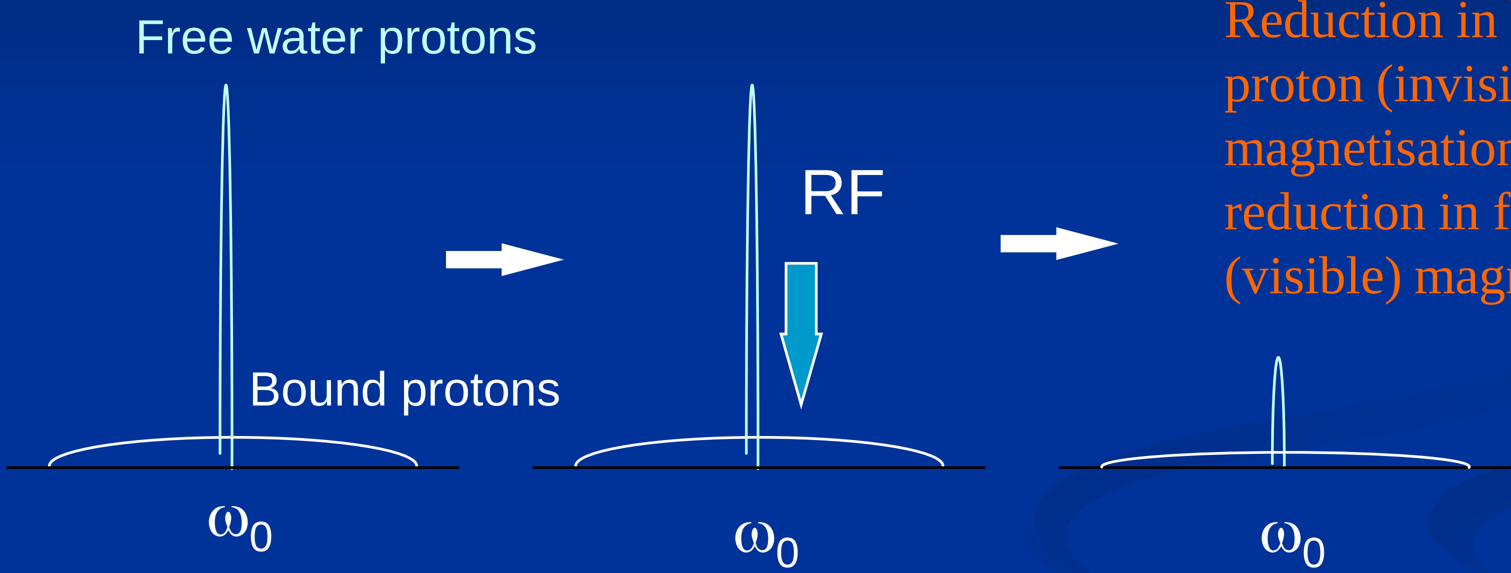

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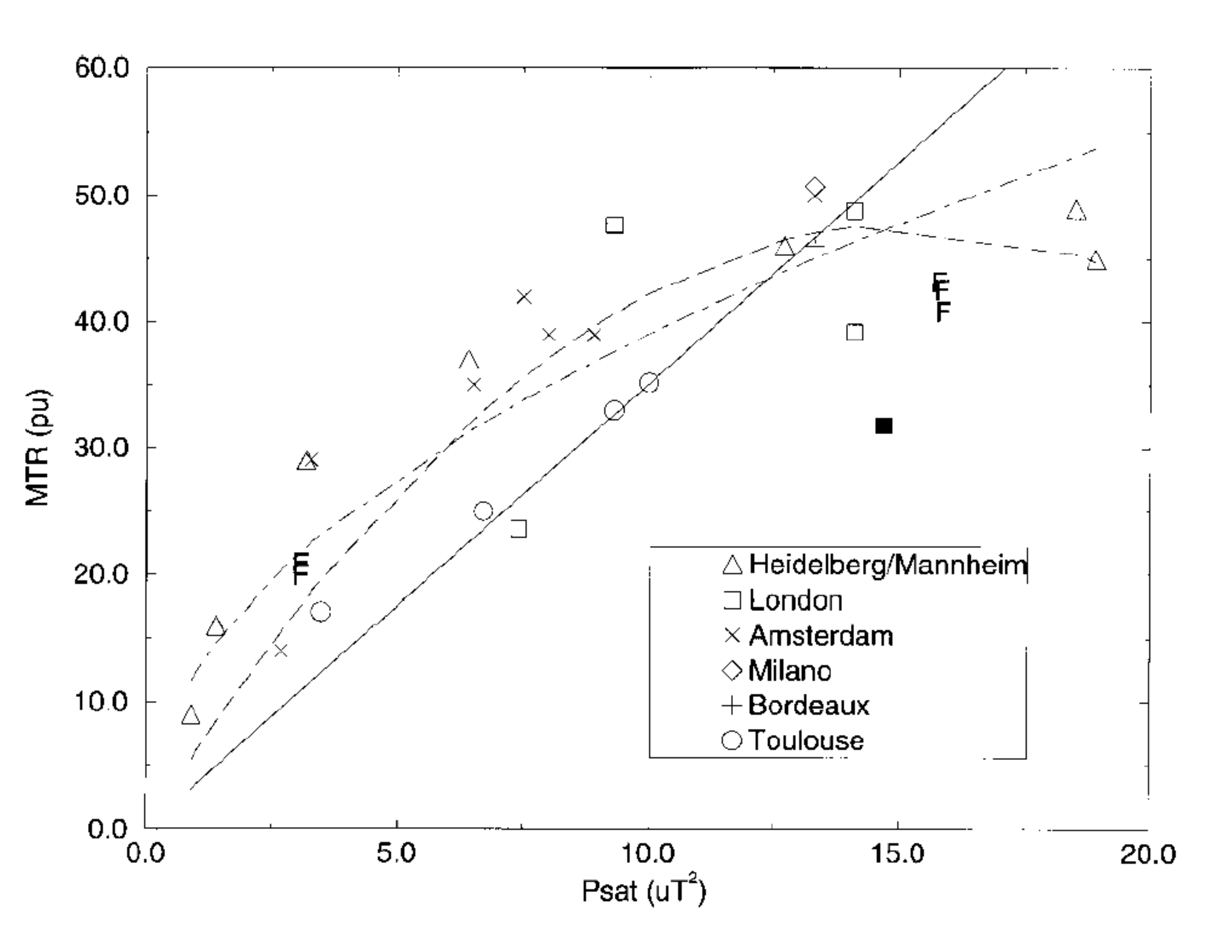
Multi-centre studies

1. Initial studies showed large inter-centre differences
2. MAGNIMS
   - MAGNetic resonance in Multiple Sclerosis
   - Subjective element reduced
     - define rules for reporting
   - Imaging procedures standardised

MTR value at 6 European centres

Berry JMRI 1999



EuroMT pulse sequence

6 Sites

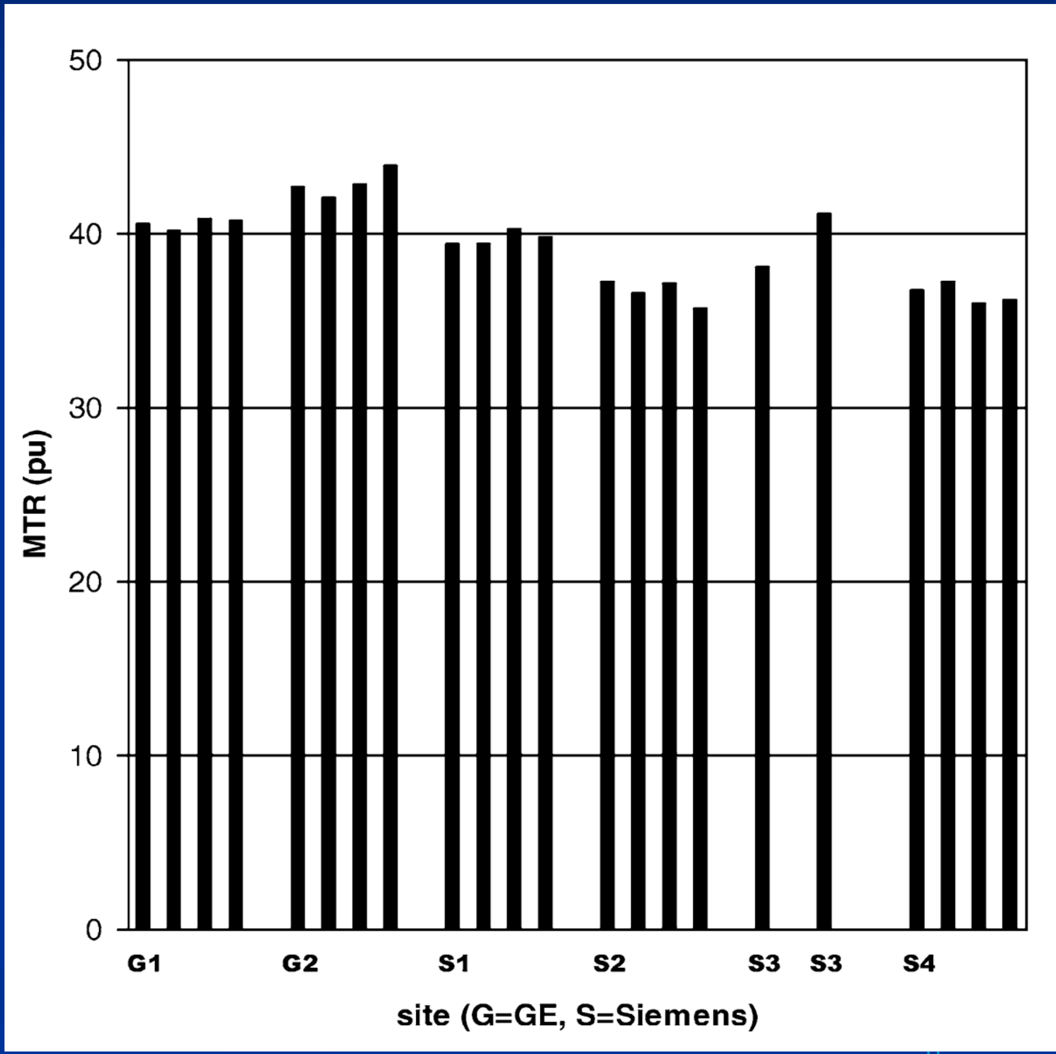
2 manufacturers

Some subjects scanned at two sites

Mean MTR value in WM closer

Inter-manufacturer difference = 3.8pu

Barker Magma 2005



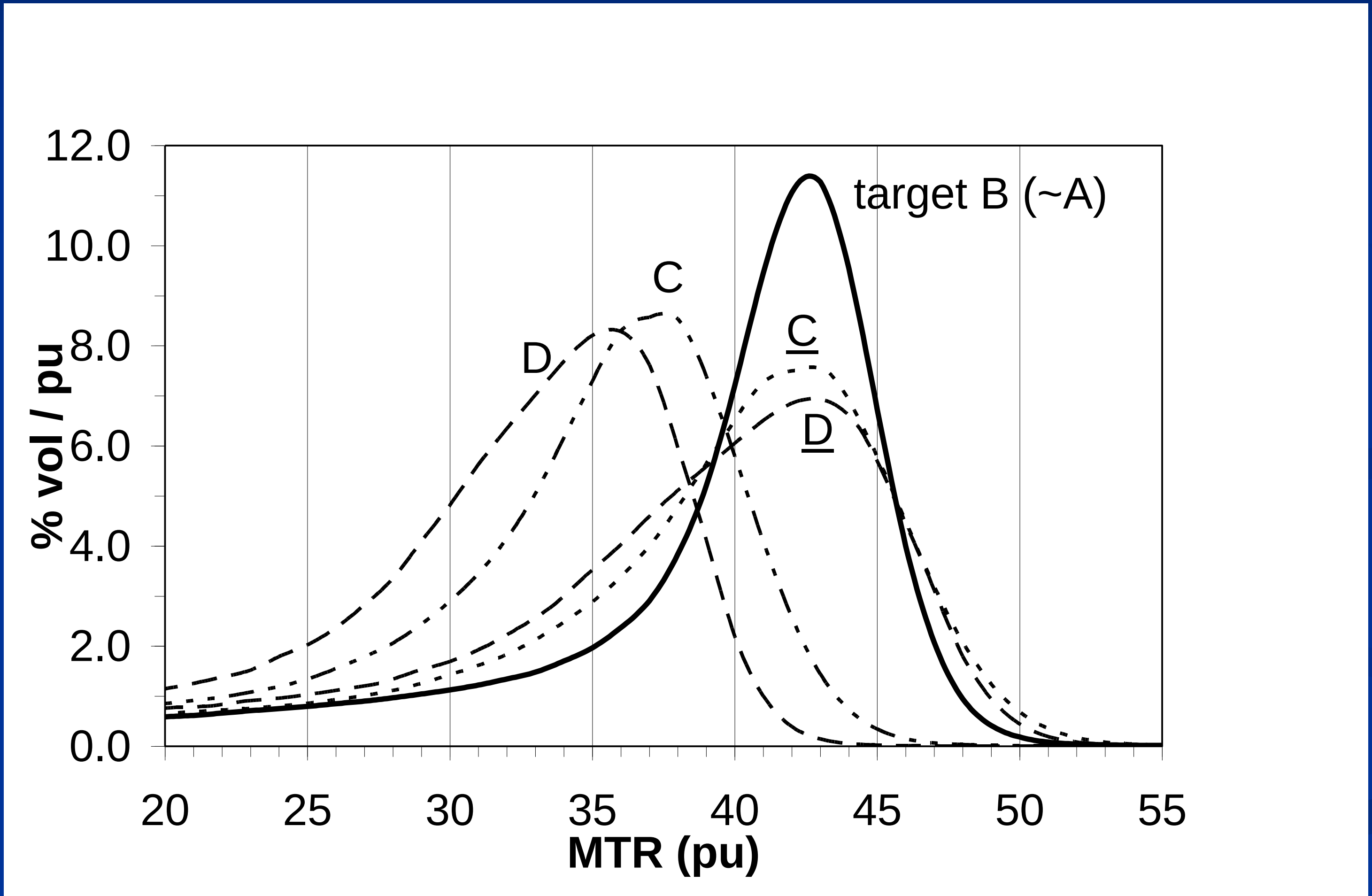
Magn Reson Mater Phy (2006) 19: 209–222
DOI 10.1007/s10334-006-0049-8

RESEARCH ARTICLE

P. S. Tofts
S. C. A. Steens
M. Cercignani
F. Admiraal-Behloul
P. A. M. Hofman
M. J. P. van Osch
W. M. Teeuwisse
D. J. Tozer
J. H. T. M. van Waesberghe
R. Yeung
G. J. Barker
M. A. van Buchem

Sources of variation in multi-centre brain MTR histogram studies: body-coil transmission eliminates inter-centre differences

MTR histograms – 4 centres



Six factors that must be controlled in a multicentre MTR histogram study

1. Transmitter coil (body or head)
2. Imager stability and setup procedure
3. MT pulse (shape, duration, offset, FA)
4. MT pulse sequence (TR', TR, imaging FA, voxel dimensions)
5. Image registration and segmentation
6. Histogram generation (bin width and labelling, normalisation)

Six factors that must be controlled in a multicentre MTR histogram study

1. Transmitter coil (body or head)

- Head coil gives non-uniform transmit field B_1
  - Broadens histogram
  - Different for each manufacturer
- Body coil gives almost-uniform B_1
- Receive coil is non-uniform
  - especially 8 channel multi-array
  - Does not matter (MTR is a ratio)
- Head gives its own NU
  - Especially at 3T
  - Same for all manufacturers

Six factors that must be controlled in a multicentre MTR histogram study

2. Imager stability and setup procedure

- Same receive gain for both MTR images
- Accurate FA setting
- Pre-scan procedure varies with manufacturer
  - Speed vs accuracy
  - Maximum at sin(90) only if TR>> T1
  - Ratio of multiple echoes
  - Which tissue location is being optimised?
  - Finding 180 is accurate and fast (but powerful)
  - Differences of ? 5-10% ? Still a fuzzy area

Six factors that must be controlled in a multicentre MTR histogram study

3. MT pulse (shape, duration, offset, FA)

- Shape – usually gaussian (sinc is too powerful)
- Some manufacturers have very little choice
- Others allow new pulse to be programmed in
- Most pulses defined by their FA (e.g. 620^{o})
- EuroMT pulse is a good starting point

Six factors that must be controlled in a multicentre MTR histogram study

4. MT pulse sequence (TR', TR, imaging FA, voxel dimensions)

- 3D sequences attractive
    - Spatial registration of M_0 and M_s possible
    - Better voxel dimensions than for 2D
    - Imaging time 3 min (2 image datasets; TR=31ms)[1]
    - Beware T_1-w; compromise with SNR

[1]**Cercignani *Neuroimage* 2005**

Six factors that must be controlled in a multicentre MTR histogram study

5. Image registration and segmentation

- CSF gives LH tails in MTR histograms
- Usually histograms come down to zero on LHS
- If necessary, this could be done at a single centre

6. Histogram generation (bin width and labelling, normalisation)

- bin labelling: ? is a 31 pu bin
  - 30.01 – 31.00 centre at 30.5
  - 30.50 – 31.49 centre at 31.0 central labelling
  - 31.00 – 31.99 centre at 31.5
  - Can give 1 pu discrepancy between centres
- Bin width
  - 1 pu often used, but can obscure peak structure
  - 0.1 pu preferred, with some smoothing
- Full normalisation
  - Divide by number of voxels
  - Divide by bin width
  - Gives absolute peak height %vol / pu

MTR histograms – 2 centres

- Using body coil transmission

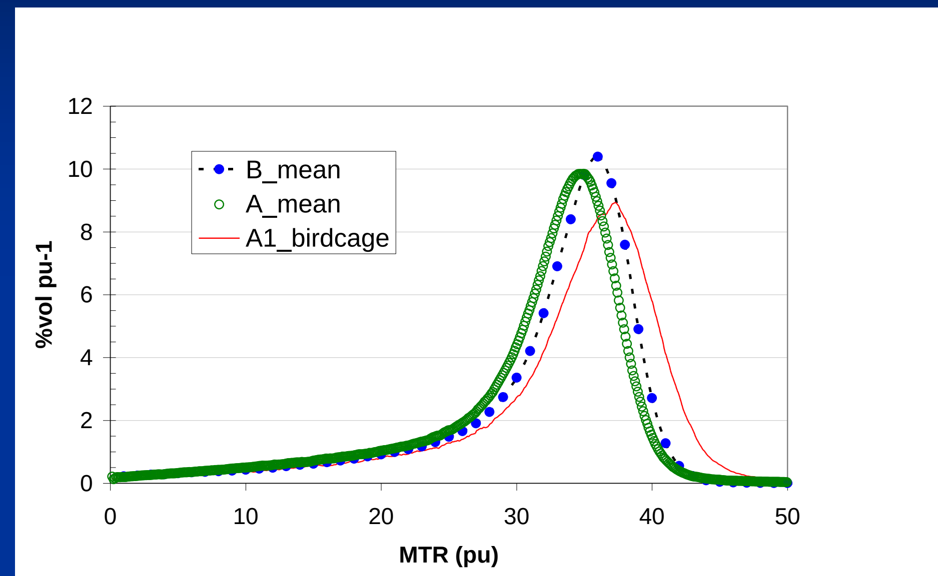
    2 centres A=Queen Square, B=Leiden (different manufacturers) agree closely

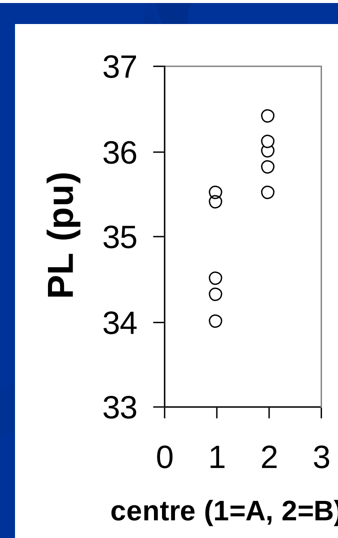
- Peak Location (PL) differs by only 1.3pu

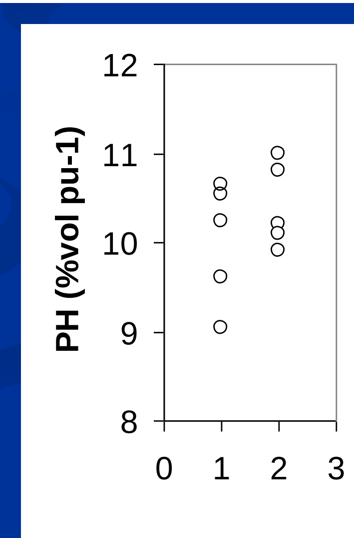
    (could be taken up in stats)

- Peak Height (PH) – ns (p=0.32)

- Birdcage head-coil shows significantly worse B_1 uniformity



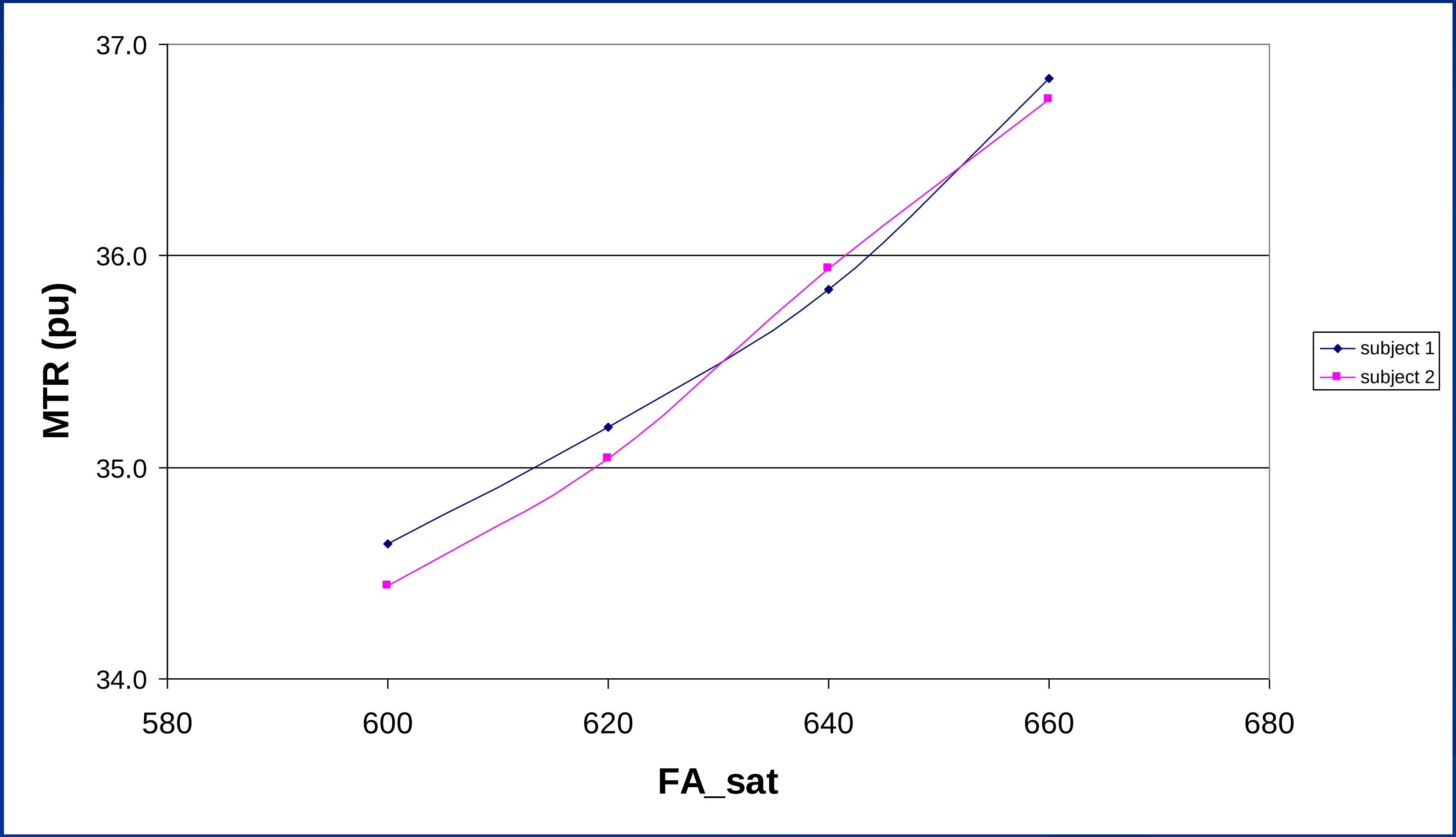




MTR histograms – 2 centres

- Remaining 1.3 pu difference between centres
- ? Caused by B_1 difference from pre-scan procedure
- Adjust FA to compensate
  - Leiden 620°
  - QS, London 652°

MTR histograms – 2 centres

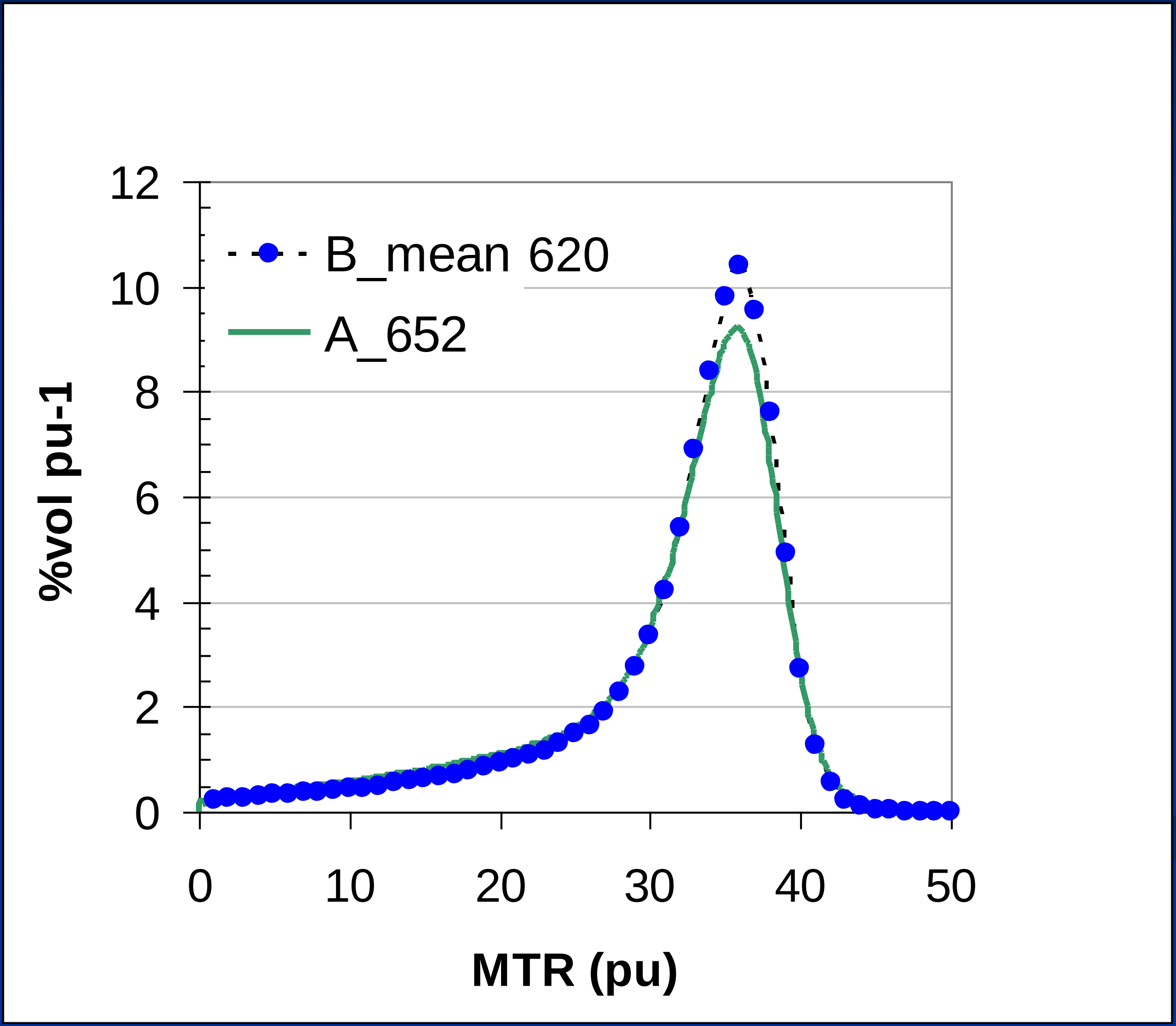


MTR histograms – 2 centres

- PL same at both sites (p=0.6)

- PH varies a little

  ? Symmetric artefact reduces PH, does not affect PL



MTR in MS

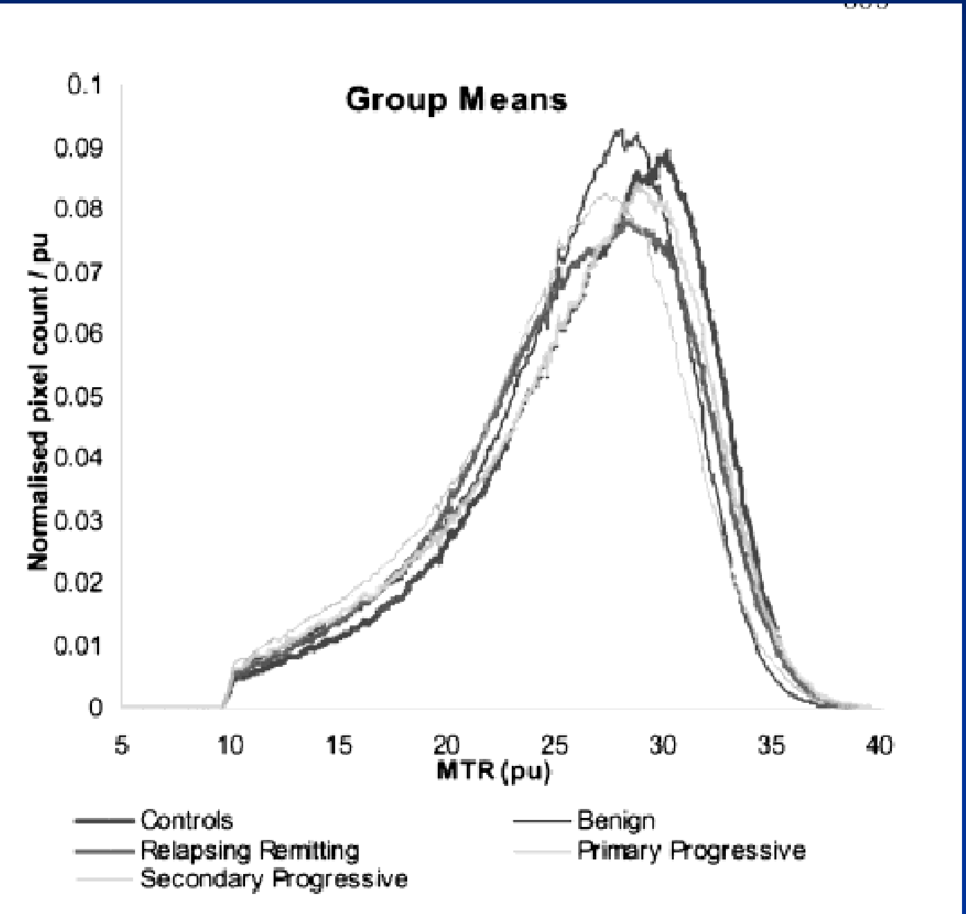
- In lesions, much reduced MTR
  - Demyelination
    - (changes fraction of restricted protons)
  - Oedema
    - Increases T_1 (see later)
  - Potential to see remyelination

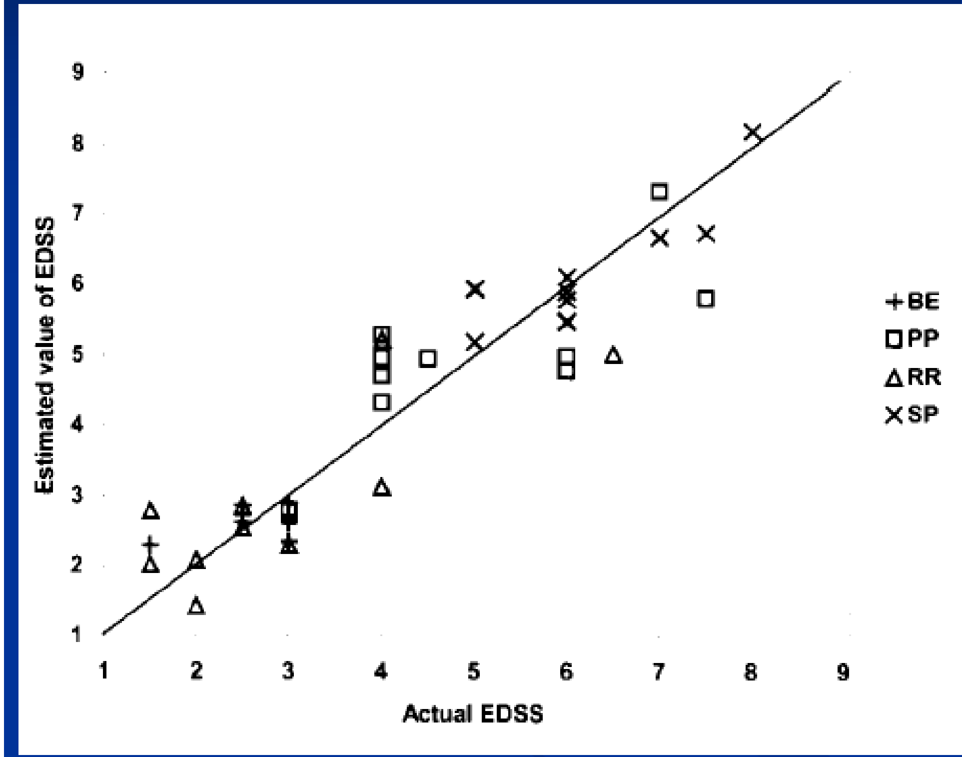
MTR in MS
normal-appearing brain tissue

MTR (pu) mean (sd)			
	MS	control	p
WM	37.8 (0.5)	38.3 (0.4)	<0.001
GM	32.0 (0.7)	32.4 (0.5)	0.004

Davies et al J Neurol 2005; 252:1037

MTR histograms in MS





Current clinical score can be predicted from histogram

(using principle components analysis - PCA)

Histogram depends on MS subtype

Dehmeshki et al MRM 2001

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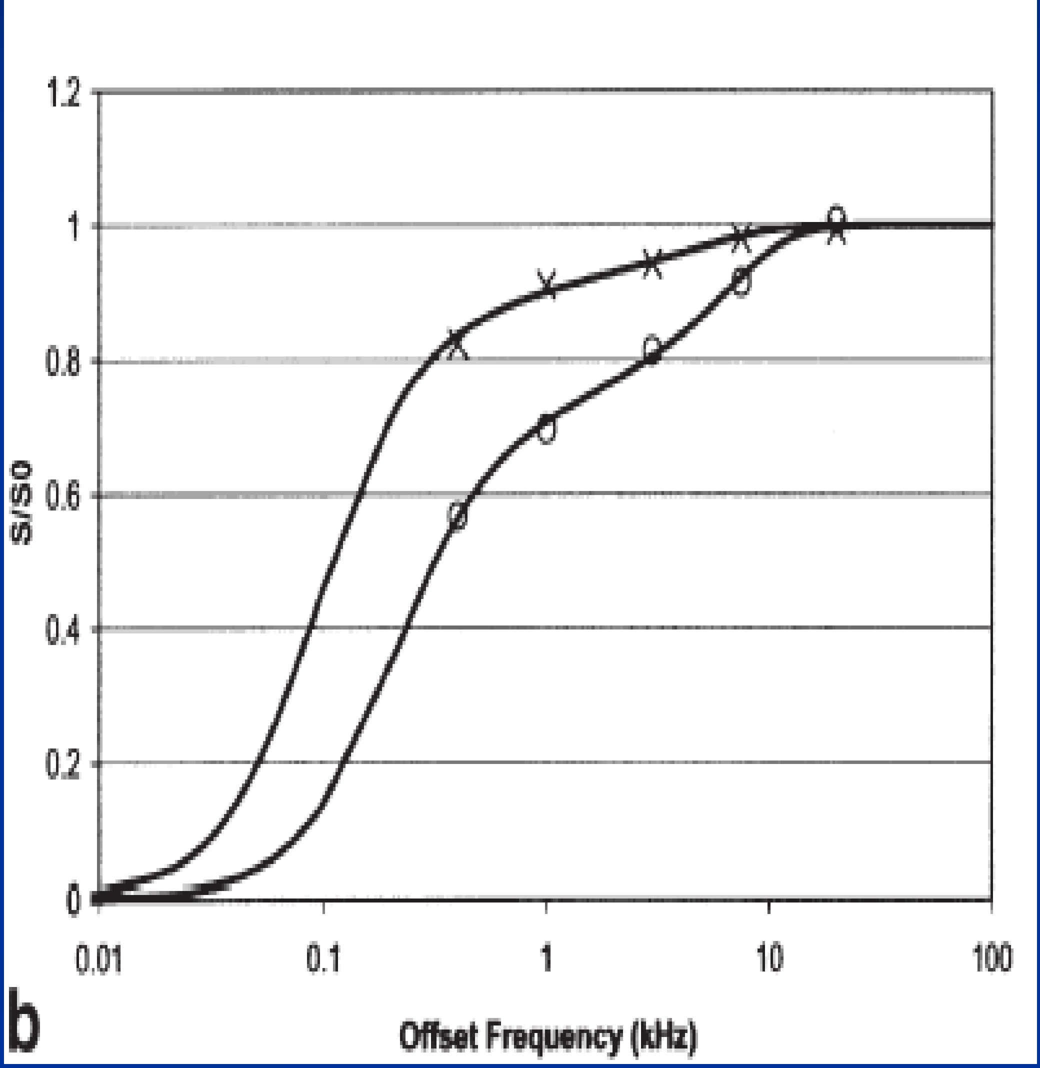
    3. Clinical applications
    4. MTR proportional to T_1 (oh dear!)

qMT

1. Measure signal reduction with range of MT pulse offset frequencies and amplitude
2. Fit complex model to these data
3. Extract parameters such as:

f_b = bound fraction of protons

(residing in macromolecules)



qMT - theory

Magnetic Resonance in Medicine 50:83–91 (2003)

Quantitative Magnetization Transfer Mapping of Bound Protons in Multiple Sclerosis

D. Tozer,* A. Ramani, G.J. Barker, G.R. Davies, D.H. Miller, and P.S. Tofts

$$S = gM_0^A \times \left(\frac{R_B\left[\frac{RM_0^A f}{R_A(1-f)}\right] + R_{RFB} + R_B + RM_0^A}{\left[\frac{RM_0^A f}{R_A(1-f)}\right](R_B + R_{RFB}) + \left(1 + \left[\frac{\omega_{CWPE}}{2\pi\Delta f}\right]^2\left[\frac{1}{R_A T_2^A}\right]\right)(R_{RFB} + R_B + RM_0^A)} \right) \quad [7]$$

a set of six parameters can be obtained from the data; these are, gM_0^A, R_B, RM_0^A, $f/R_A(1-f)$, $1/R_A T_2^A$, and through the lineshape, R_{RFB}, T_{2B}.

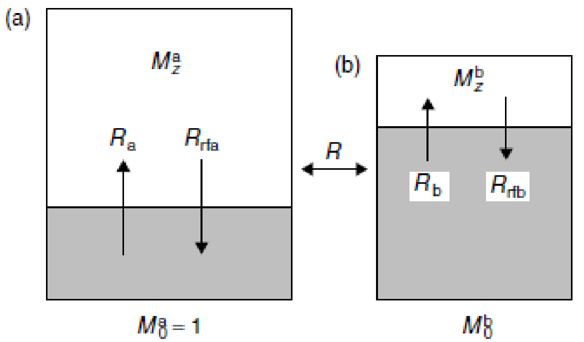


Figure 8.2. A model of a two-pool system, with exchange. The shaded part of each pool represents magnetization which is not aligned longitudinally. R_a and R_b are the longitudinal relaxation rates ($R = 1/T_1$), which enable longitudinal magnetization to recover. R_{rfa} and R_{rfb} are the saturation terms which destroy longitudinal magnetization. R is the exchange between the pools. (a) Liquid; (b) semisolid. Reproduced with permission from Henkelman RM, Huang X, Xiang QS, Stanisz GJ, Swanson SD, Bronskill MJ, Quantitative interpretation of magnetization transfer, in *Magn. Reson. Med.*, Copyright 1993; John Wiley & Sons Inc.

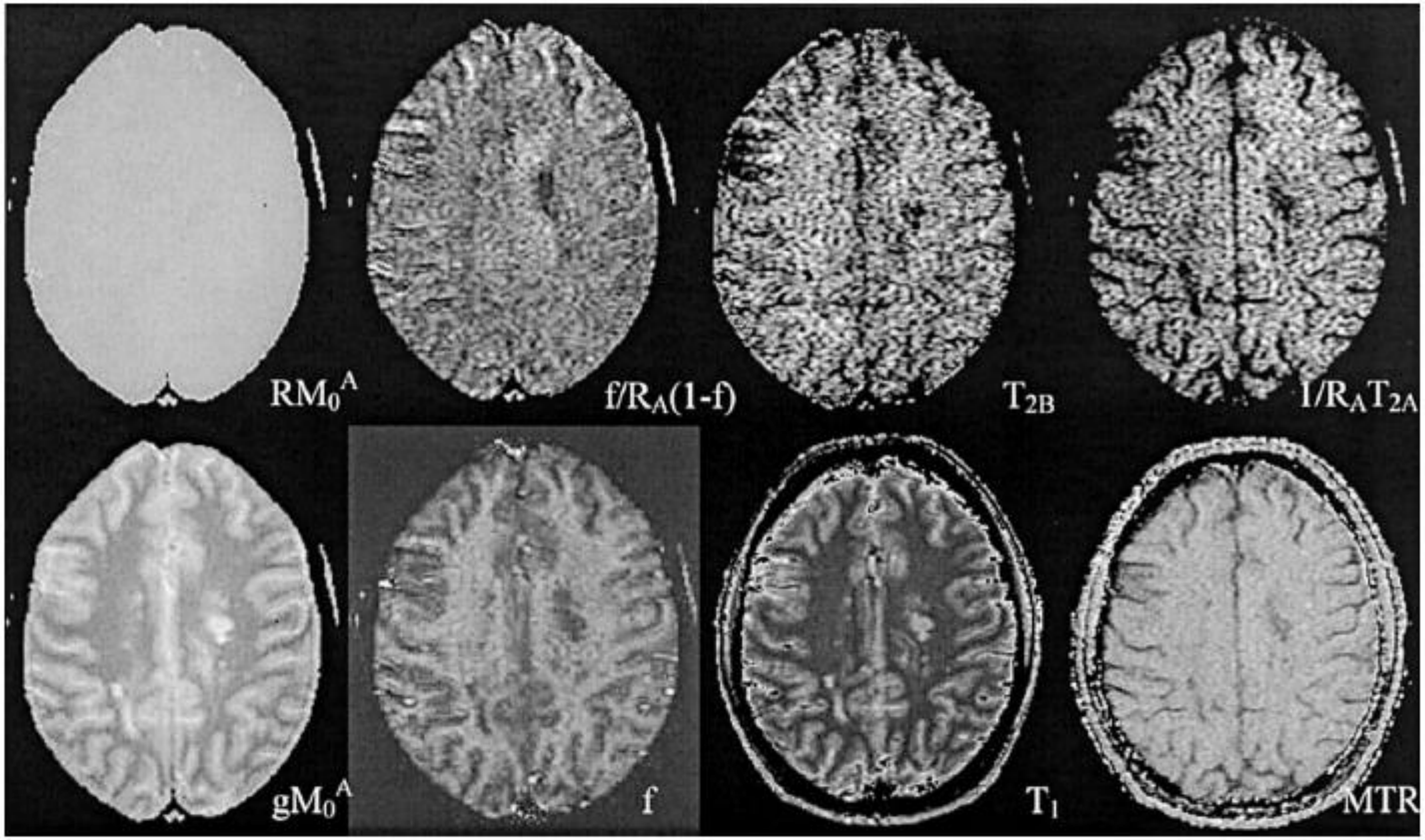


FIG. 2. A series of parameter maps obtained from an MS patient. As can be seen, the lesions visible on gM_0^A in the left centrum semiovale and posterior right of the brain are visible particularly well on $1/R_AT_{2A}$ and f, and also to a lesser extent on $f/R_A(1-f)$ and T_{2B}. The T_1 and MTR maps also show these lesions, but the shape of the left centrum semiovale lesion in particular seems to vary—it appears bigger on the f and $1/R$ R_AT_{2A} maps than on the T_1 map, indicating an abnormality surrounding the conventional lesion. Also, note the small lesions visible on gM_0^A and f, which are not as clear on the T_1 and MTR maps.

gM_o^A = PD;   f=bound fraction

qMT in MS

Frontal WM	f_b	p
Control	9.8	
NAWM	8.6	<0.01
Lesion	4.6	<0.01

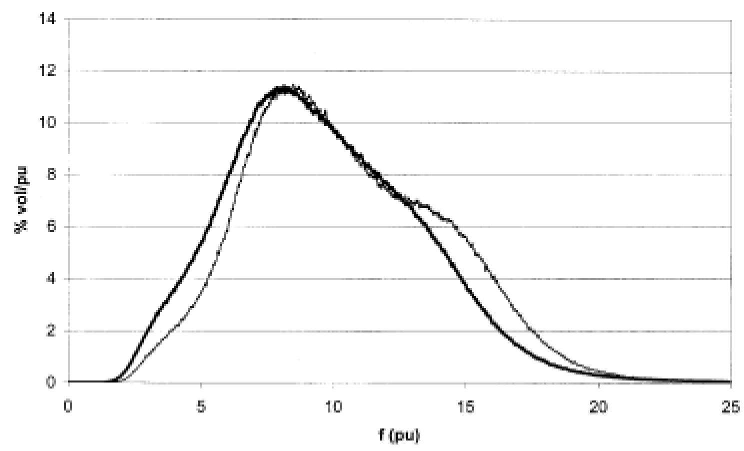
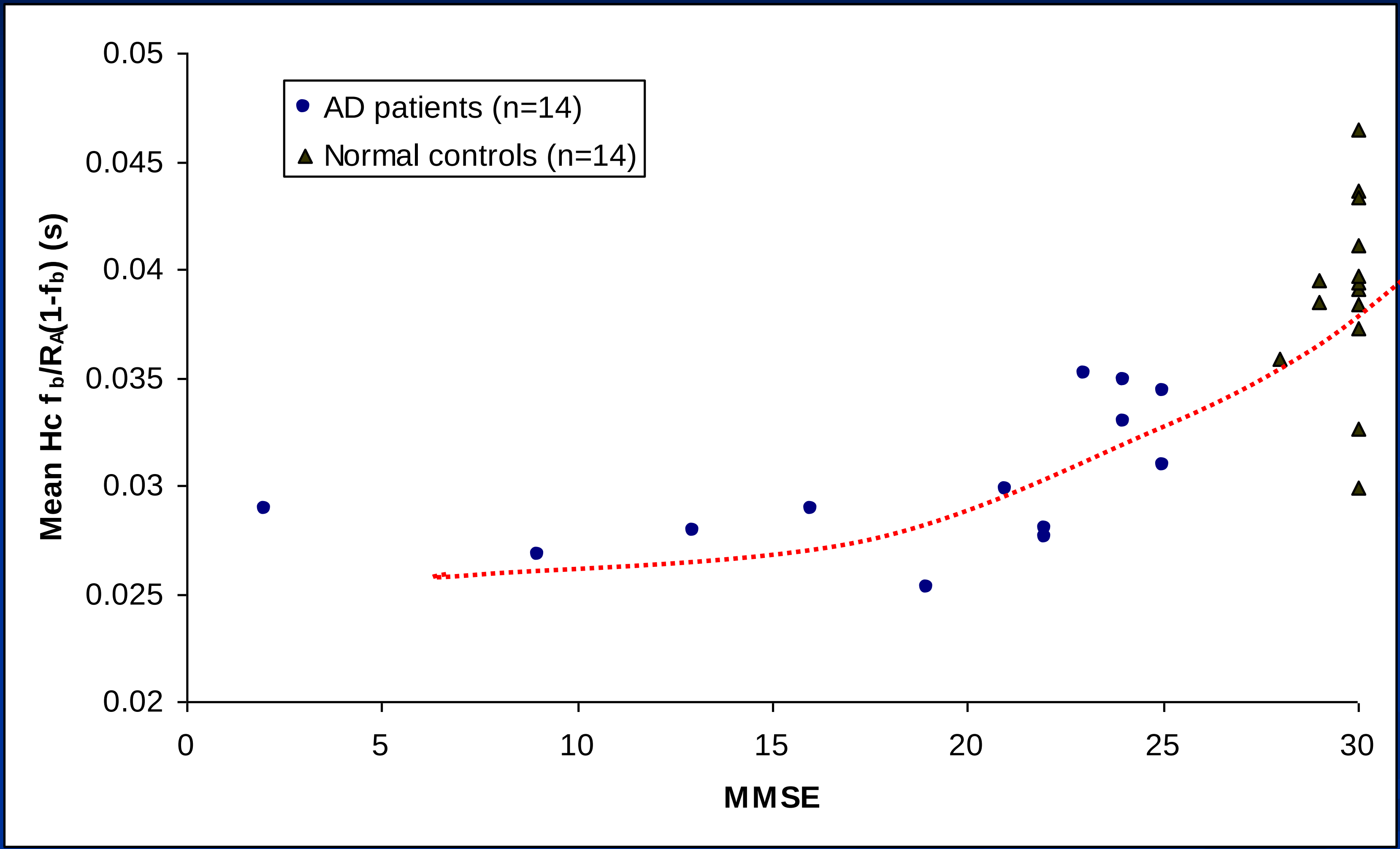


FIG. 3. Group histograms for the bound proton fraction, f. The thicker line represents the patient group (n = 20) and the thinner line the control group (n = 7). Note the increased height of the patient histogram at smaller values of f, due to the reduced value of f in NAWM and possibly the presence of lesions.

Davies et al Mult Scler 2004; 10:607

Alzheimer's disease



Hippocampal qMT parameter (~ f_b) vs clinical score

Ridha, Fox, Tofts. Quantitative magnetization transfer imaging in Alzheimer disease Radiology 2007; 244:832

ELSEVIER

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 27 (2005) 436 – 441

Three-dimensional quantitative magnetisation transfer imaging of the human brain

Mara Cercignani,[a,*] Mark R. Symms,[b] Klaus Schmierer,[a] Philip A. Boulby,[b] Daniel J. Tozer,[a] Maria Ron,[a] Paul S. Tofts,[a] and Gareth J. Barker[c]

[a]*Department of Neuroinflammation, NMR Research Unit, 6th floor, University College London, Queen Square House, Institute of Neurology, Queen Square, London WC1N 3 BG, UK*
[b]*Department of Clinical and Experimental Epilepsy, Institute of Neurology, University College London, London WC1N 3BG, UK*
[c]*Centre for Neuroimaging Sciences, Department of Neurology, Institute of Psychiatry, Kings College London, London SE5 8AF, UK*

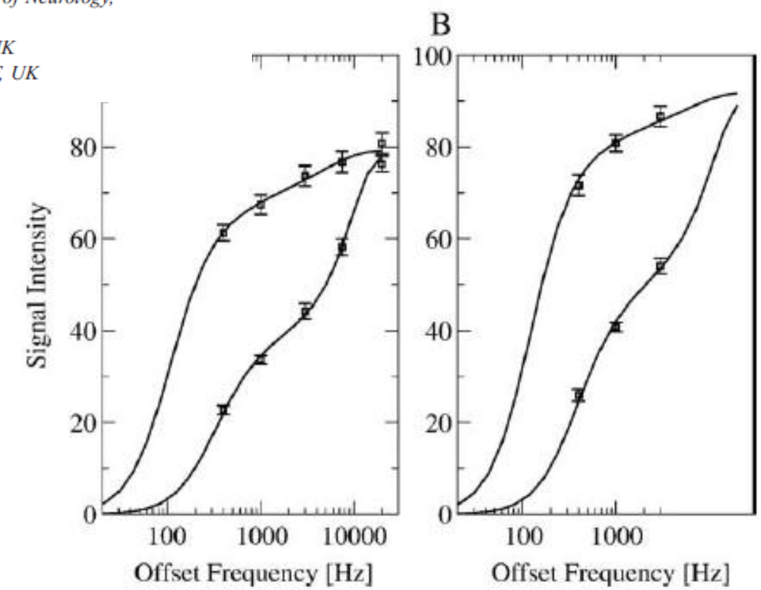


Fig. 3. Typical curves obtained by fitting the 10 MT-weighted mean signal intensities (squares) measured in manually drawn regions positioned in the posterior limb of the left internal capsule (A) and in the right thalamus (B). The error bars show the standard deviation of signal intensity (arbitrary units) within the region. The residual error was 1.1% for the internal capsule and 1.2% for the thalamus.

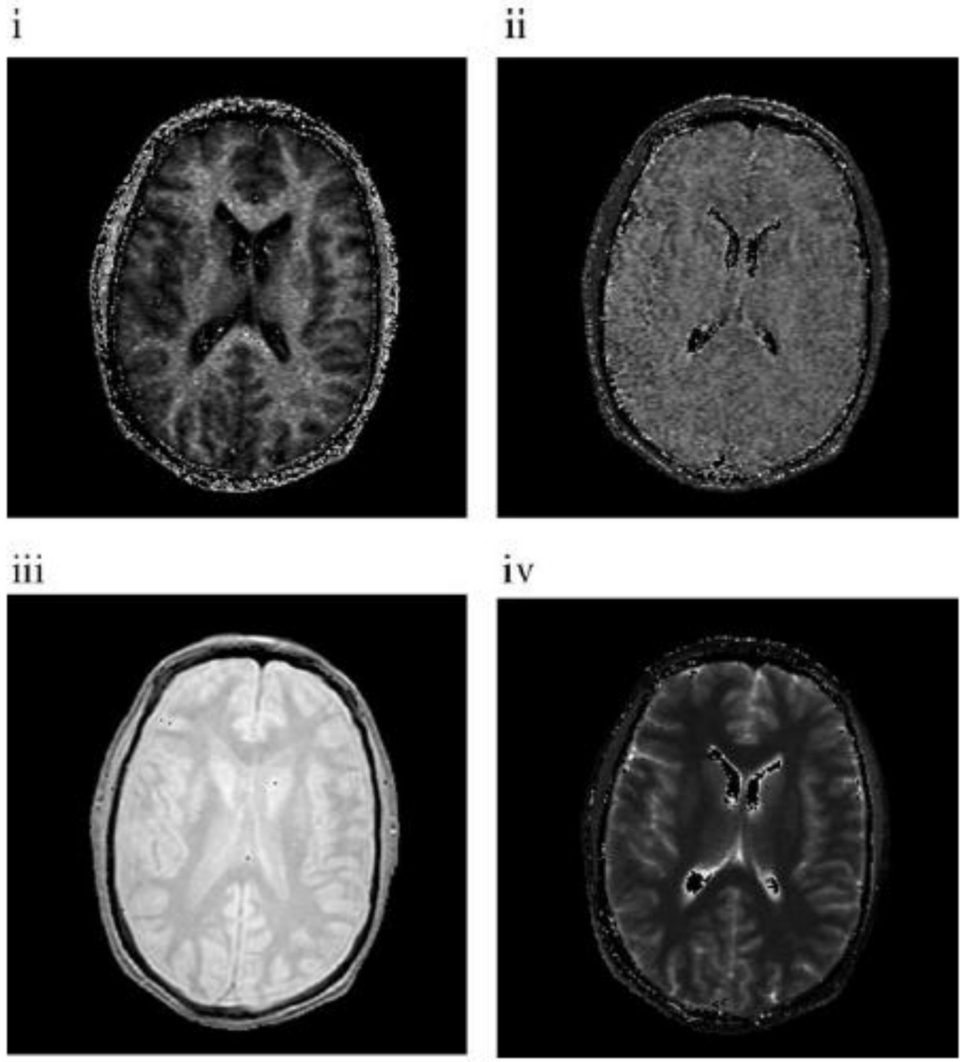


Fig. 2. Typical quantitative MT parametric maps obtained from a healthy subject using the 3D-MTSPGR acquisition described in the paper: macromolecular proton fraction, f (i); transverse relaxation time of the semisolid pool, T_2^B (ii); proton density, gM_0^A (iii); and longitudinal relaxation time of the free pool, T_1^A (iv).

qMT - optimisation

1. Measure f_b only (not other qMT parameters e.g. T_{2b})
2. Adjust (optimise) values of MT pulse offset and amplitude
3. Noise in f_b map reduced by 30% (compared to standard protocol)
4. Or **exam time reduced by 50%**
5. Generic problem – optimise acquisition parameters for given task

Samson et al ESMRMB 2005; ISMRM 2006

Q: do myelin estimates from qMT and multiple-T2 agree?

A: Positive correlations were seen for

MS lesions (r ~ 0.2) and in

WM in patients (r ~ 0.6)

Low correlations; 2 parameters give independent information

Is this expected / unexpected …….???

Correlation of Apparent Myelin Measures Obtained in Multiple Sclerosis Patients and Controls From Magnetization Transfer and Multicompartmental *T*2 Analysis

D.J. Tozer, G.R. Davies, D.R. Altmann, D.H. Miller, and P.S. Tofts Magnetic Resonance in Medicine 53:1415–1422 (2005)

MT in PM tissue
Klaus Schmirer

	MTR	T_1	f_b
Fresh NAWM	33.9	667	7.1
Fresh lesion	24.5	1195	3.0
Fixed NAWM	30.0	377	10.8
Fixed lesion	22.5	747	4.3
Fixing WM (%)	-11	-43	53
Fixing lesion (%)	-8	-37	43
Demyelination fresh (%)	-28	79	-58
Demyelination fixed (%)	-25	98	-61

MTR depends on T_1

	MTR	T_1	f_b	R_{rfb}[1]
Fresh WM	33.9	667	7.1	7.2
Fresh lesion	24.5	1195	3.0	6.9
Fixed WM	30.0	377	10.8	7.4
Fixed lesion	22.5	747	4.3	7.1
Fixing WM (%)	-11	-43	53	
Fixing lesion (%)	-8	-37	43	
Demyelination fresh (%)	-28	79	-58	
Demyelination fixed (%)	-25	98	-61	

[1] **$MTR \sim= R_{rfb}\ T_1\ \ f_b$**

Lee and Dacher JMRI 1997 and Tofts *QMRI of the brain* 2003

The future

1. qMT for ‘bound fraction’ f_b
   - more specific than MTR
   - Harder to implement; ?needs T_1
   - International consensus on terms, modelling, implementation
2. Multi-echo – ‘myelin water’
   - specific?
   - restricted coverage and hard to implement

Acknowledgements: Multi-centre MTR histograms:
Stefan Steens, Mark van Buchem
Dan Tozer, Mara Cercignani, Gareth Barker