Measuring the invisible using Quantitative MRI: a vision of the future

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Four questions

1. Why should we **Quantify**?
2. Why are **repeatability** and **reproducibility** important?
3. What is a **Perfect qMRI Machine?**
4. What is the proposed **MRI medal system**?

Quantification

- Quantify – to measure a quantity (size, weight, blood sugar, cholesterol …)
- Medical images have been *qualitative*
  - **Look**; human assessment; experience needed
- Imaging is becoming *quantitative*
  - **Measure** e.g. tumour size, water content, tissue destruction, volume of MS lesions…

Why does random error matter?

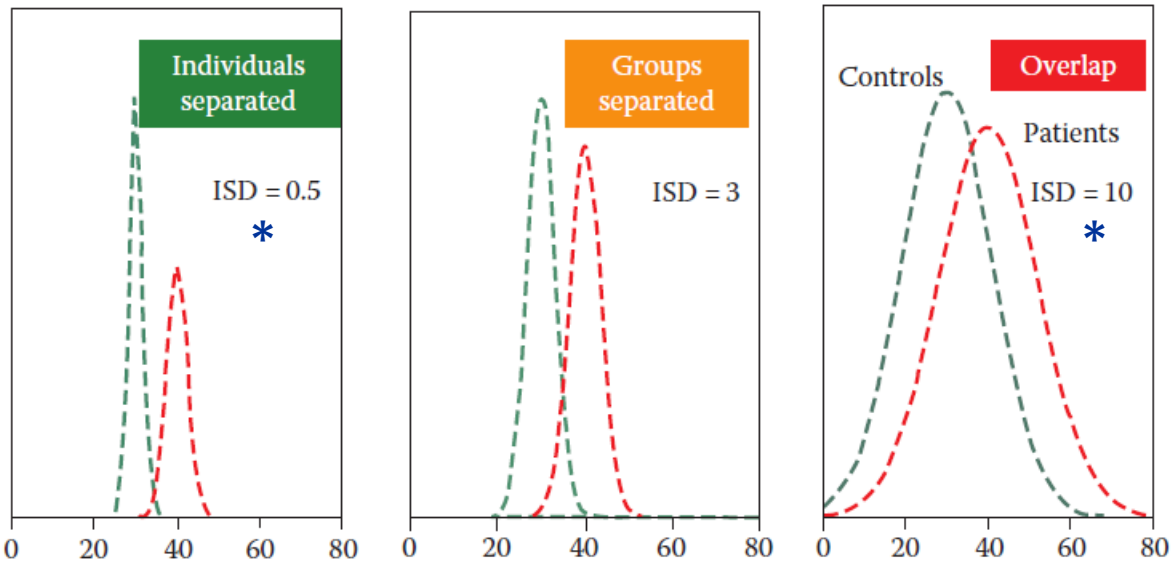


FIGURE 3.5A Simulation showing how magnitude of ISD affects ability to use an MR parameter to separate groups and individuals. Group separation is 10 units. With ISD = 10 (right-hand image), the groups overlap, and considerable statistical power would be needed to separate them (see Chapter 1, Figure 1.3). A reduced ISD = 3 (centre) gives a good group separation c) a further reduction to ISD = 0.5 (left-hand image) enables individuals to be accurately classified into their group.

* ISD = Instrumental Standard Deviation (repeatability)

Why is repeatability important?

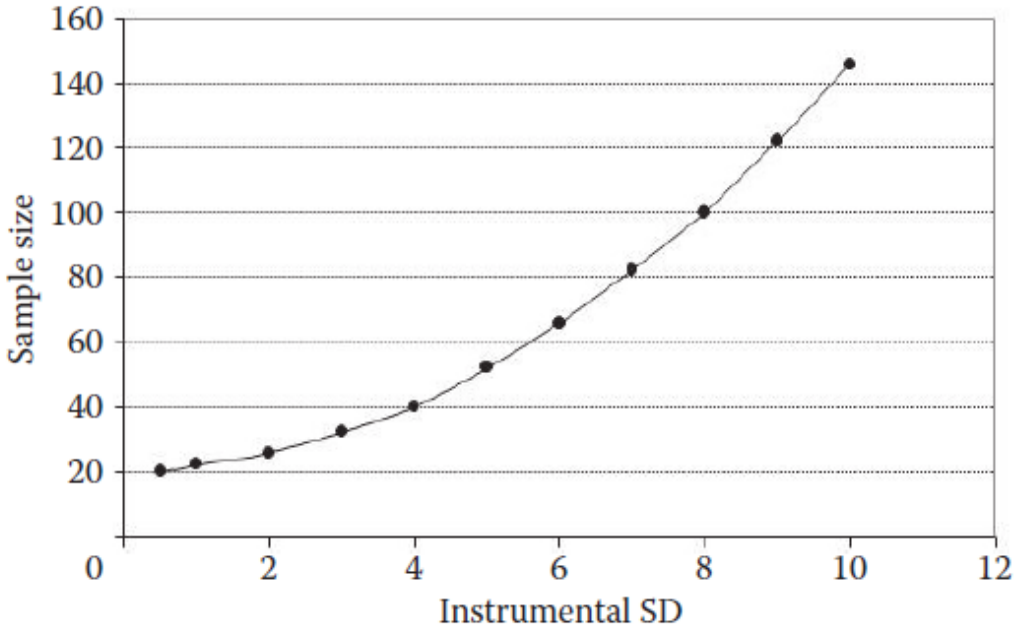
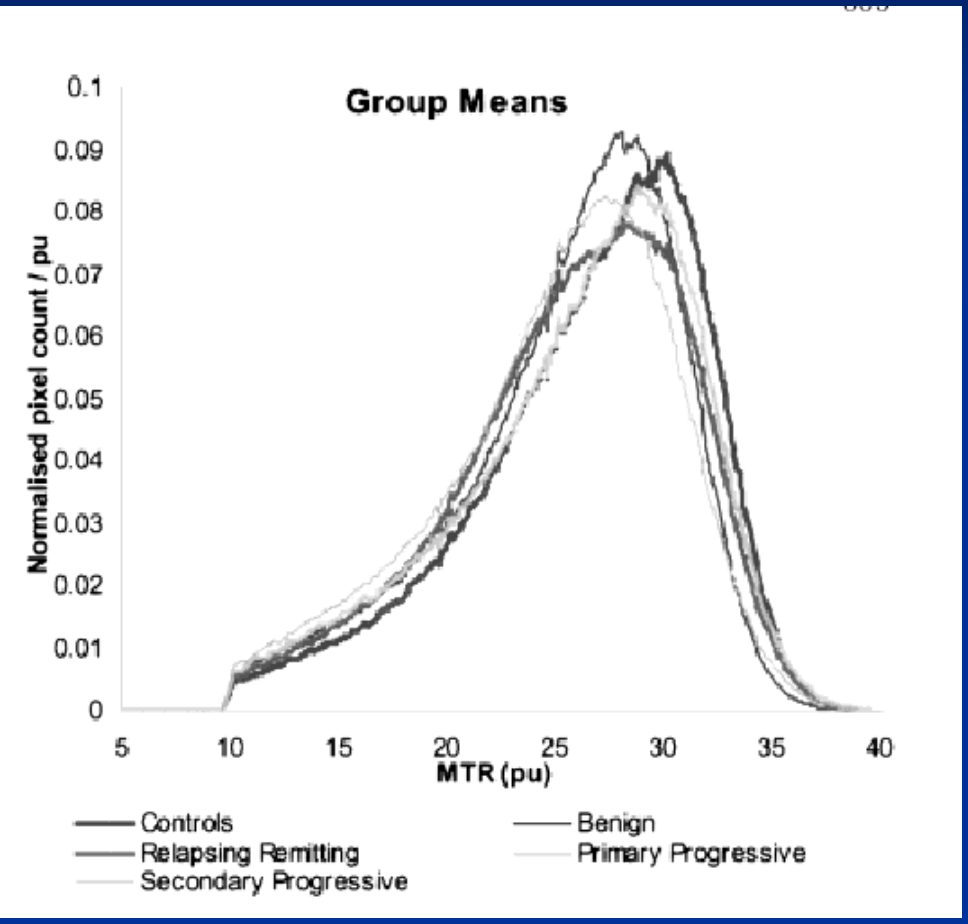
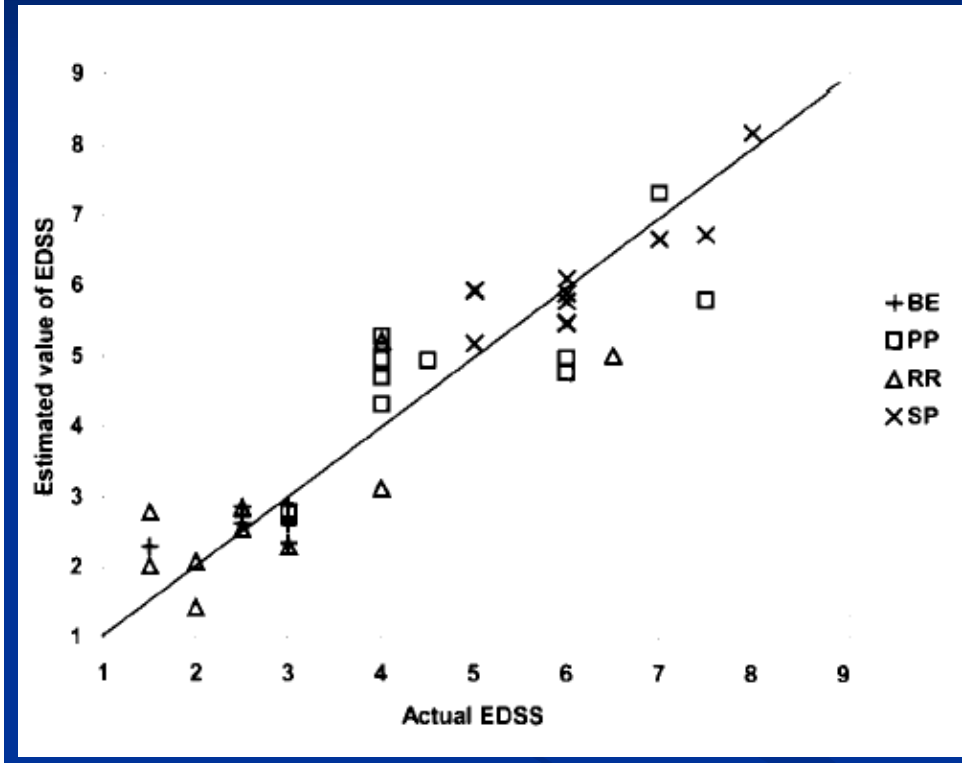


FIGURE 1.3 The effect of instrumental precision (ISD) on the power of a study and the required sample size. By reducing the ISD, the sample size required is dramatically reduced, with a consequent saving in the cost and duration of the study. This is a simulation based on group comparison between controls (parameter value mean = 100, SD = 3) and the same number of patients (effect size = 5, SD = 4.25). Power P = 80%, significance level $\alpha = 0.05$, using G*power3 which is an established software that can be downloaded free of charge.

MTR histograms in Multiple Sclerosis



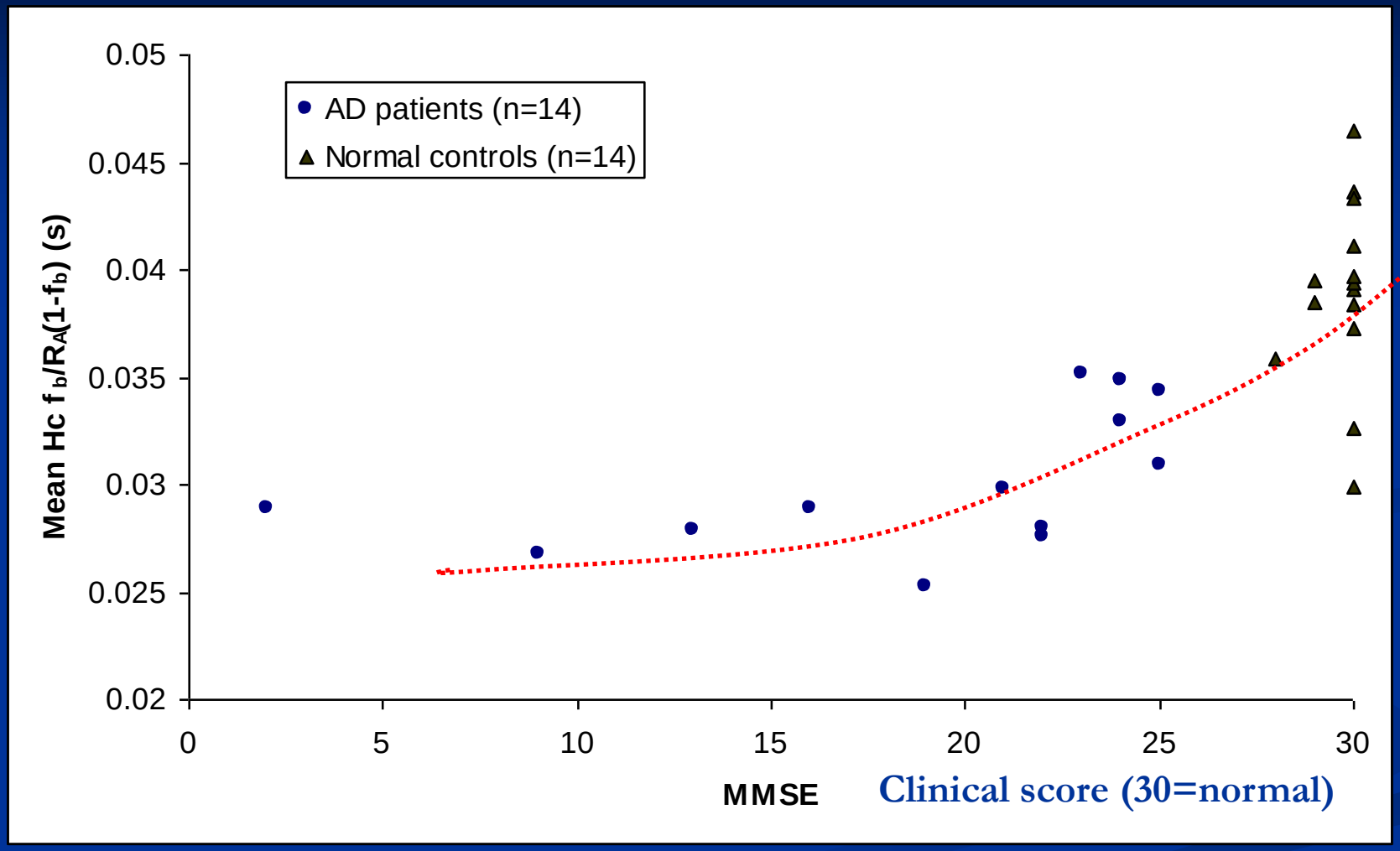


Current clinical score (EDSS) can be predicted from histogram (using principle components analysis - PCA)

Whole-brain histogram depends on MS subtype; sensitive to demyelination

Dehmeshki Tofts Magn Reson Med 2001

Alzheimer's disease



Hippocampal qMT parameter (~ myelin concentration) vs clinical score

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

Perfection is possible

A Perfect Quantitative MRI machine is one that, in making a measurement, contributes no significant extra variation to that which already exists from biological variation.

The concept of the 'Perfect Machine' originates in the building of the 200 inch Palomar telescope in 1933-48.

inspiration: In Thomas Mann's *Death in Venice*, the writer is on the Venice beach. He sees the detail, in the foreground: children constructing a sand castle. He turns his gaze to the horizon, empty and infinite. What would it be to be a measurement hero?

From ***Quantitative MRI of the Brain*** p10

Medals for Perfection

TABLE 1.3 qMRI Medals for Perfect Machines: A Proposal

Medal	Target Study	Criterion	Motivation
Bronze	Group comparison	ISD < 0.3 GSD	(a)
Silver	Multicentre study	BCSD < GSD	(b)
Gold	Serial study	ISD < 0.3 WSSD	(c)

Note: SD: standard deviation; BSD: biological SD; GSD: group SD; ISD: instrumental SD; ICSD: inter-centre SD; BCSD: between-centre SD; WSSD: within-subject SD.

[a] In a group comparison, within-group variation GSD^2 should dominate (i.e. machine variation ISD makes an insignificant contribution to total within-group variation).

[b] The effect of between-centre variation (BCSD) should be less than within-group variation.

[c] In a serial study, total within-subject variation $WSSD^2$ should dominate (i.e. machine variation ISD makes an insignificant contribution to total within-subject variation).

NB A medal could exist for each qMR parameter.
Inspiration: the lifetime work of John Harrison, who constructed stable travelling clocks. The Longitude prize of £20k was offered by the British parliament in 1714, in response to loss of life at sea and an urgent need for better navigation. This medal scheme might be attractive to a philanthropist.
from *Quantitative MRI of the Brain* p10

Normal range depends on repeatability

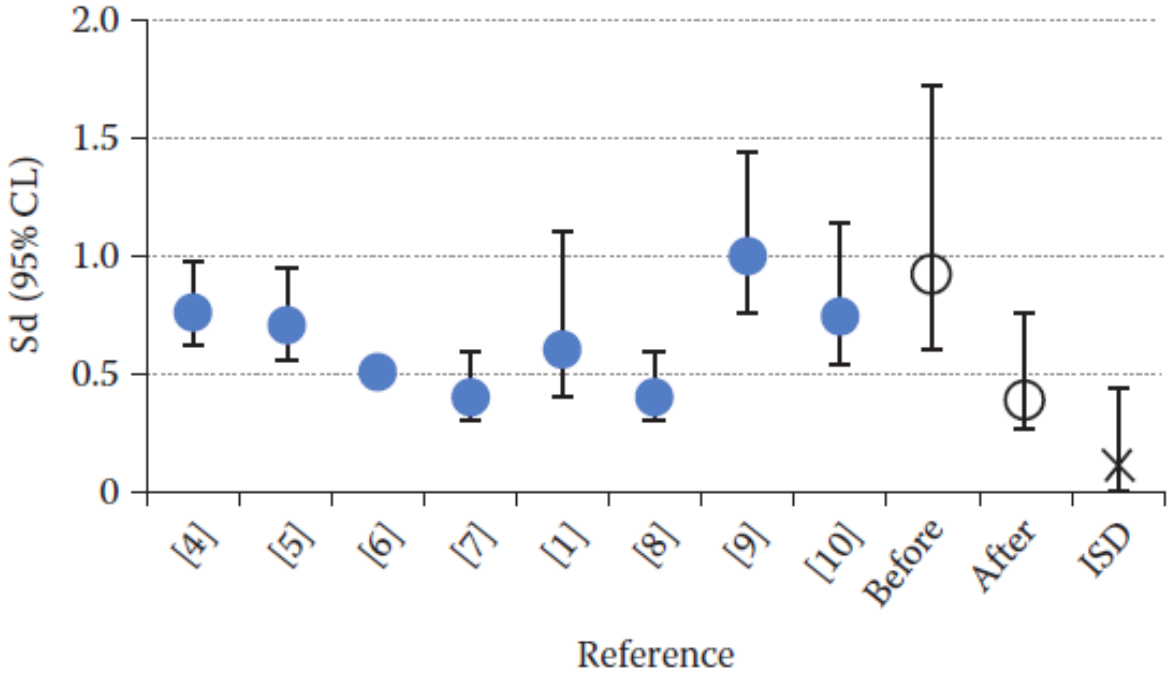


FIGURE 3.8 Normal variation for white matter MTR, and influence of ISD. Blue circles are published values of SD (units for MTR are pu; mean was 38–40 pu) from eight centres; error bars show uncertainty in sd estimate (Equation 3.2). *Before* is authors' first value, almost the highest value of nine centres. After solving a scanner instability problem (Figure [stability] in Chapter 2), ISD was low (≃0.2 pu) and the re-measured normal range (*after)* dropped to the lowest value of nine centres.

Reproducibility across centres

1. Much work on multi-centre studies (e.g. MAGNIMS 1990's)
   EU funded MAGNetic resonance Imaging in Multiple Sclerosis)

2. 'Protocol Matching' across different manufacturers using standard clinical sequences
   Works for simple parameters (T_1, D, MT)
   Relatively easy to implement on a wide scale

3. Complex parameters (e.g. DCE K^{trans}) are often in a 'black box' and may need 'open source' software run on each maker's machine
   May need Research Agreement for each machine

4. National Measurement centres: use their expertise and concepts
   NIST – National Institute of Standards and Technology, USA
   PTB - National Metrology Institute of Germany
   NPL – National Physical Laboratory, UK

Between-centre difference can be eliminated

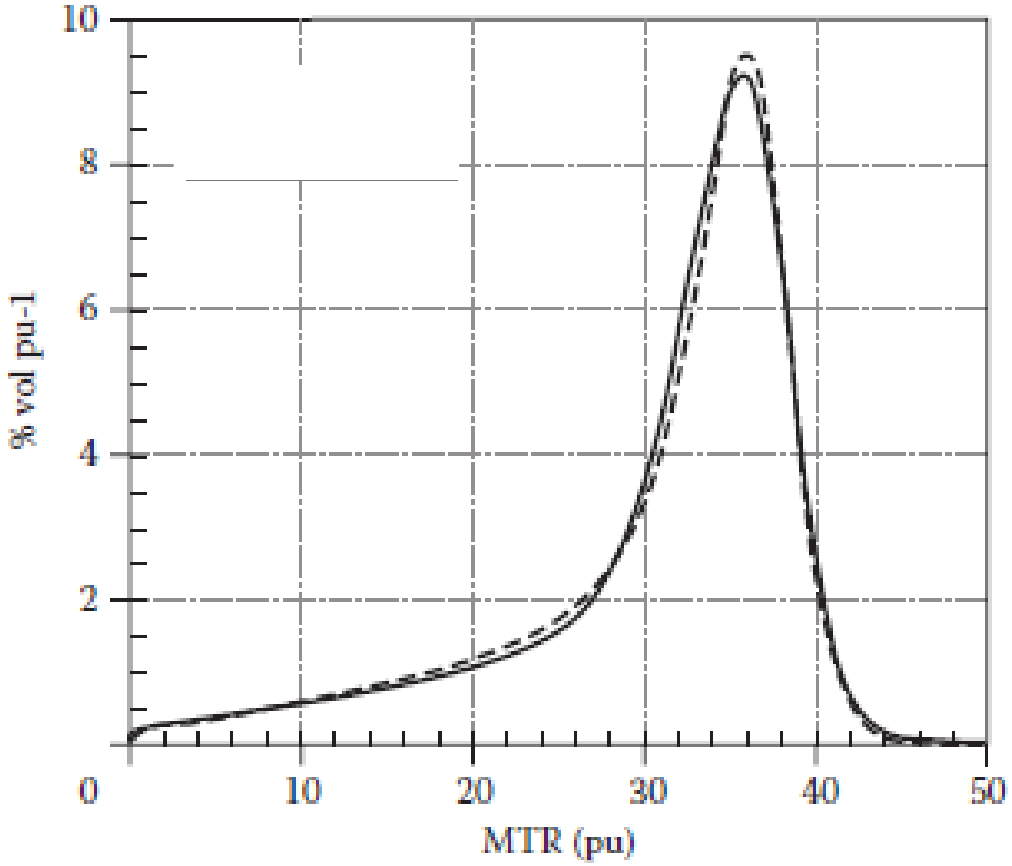


FIGURE 2.9 Matching MTR group histograms from two centres with 1.5T scanners from different manufacturers. By using body coil excitation and standardised histogram generation, inter-centre differences were eliminated. (From Tofts, P.S., *et al.*, *Magma*, 19(4), 209–222, 2006.)

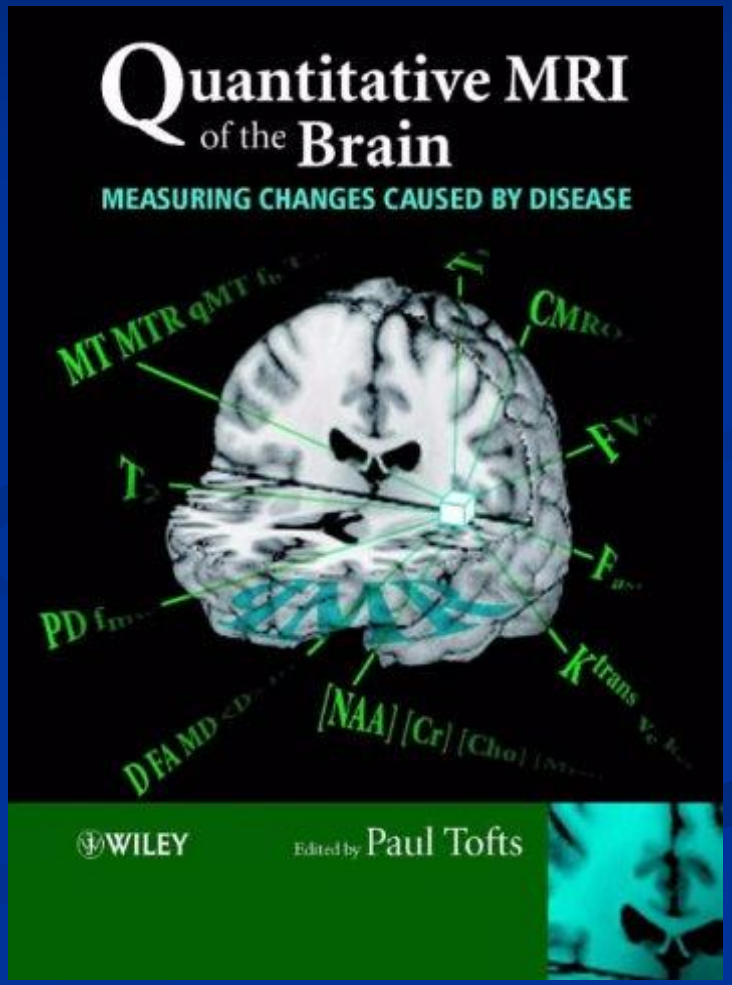
qMRI – a technology whose time has come

Medical Imaging

meets

Measurement Science

British Medical Association Radiology book prize 2004



'The pre-eminent role of imaging now requires a new level of metric - quantitative measurements'

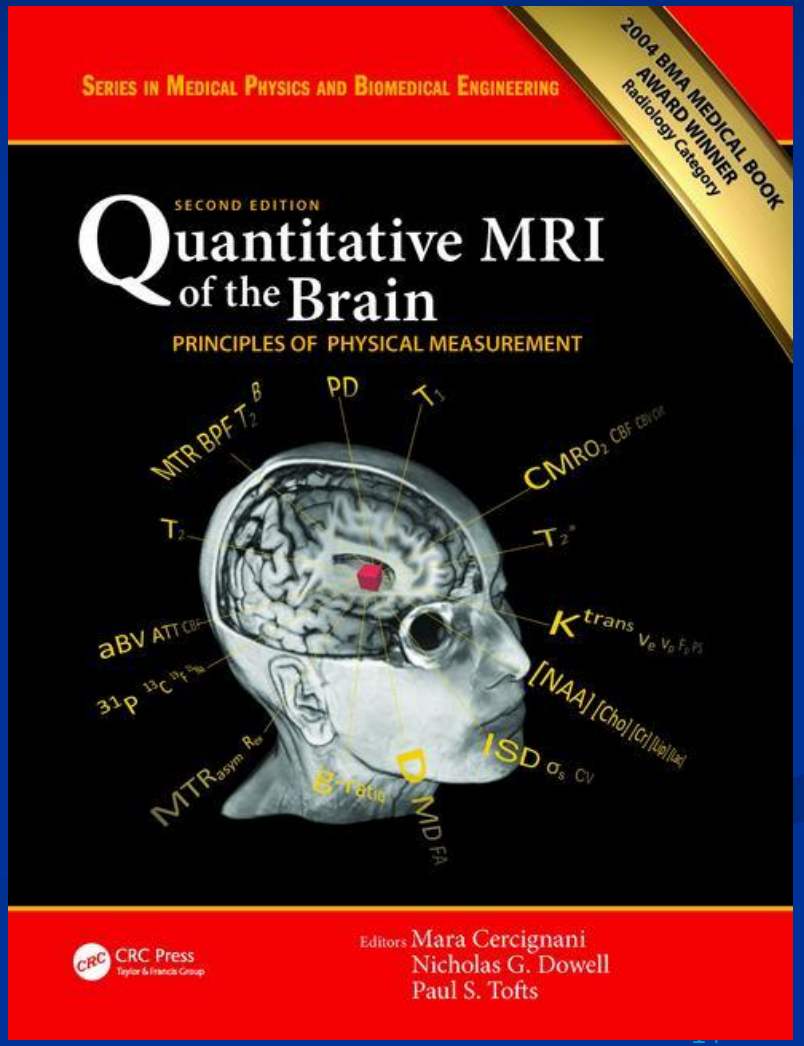
Robert I Grossman MD, Chair of Radiology, New York University

New edition 2018

€150 hardback; €50 eBook (CRC press)

see qmri.org (some author pre-prints)

Contents



Why is qMR needed?

1. Measurement concepts - sources of variation
2. Specificity - new biological quantities
3. Scientific instrument following long tradition of measurement in astronomy, physics, chemistry, electrical engineering…
4. Measure subtle 'invisible' changes ; diffuse or small, in 'Normal-Appearing' brain tissue

qMR – the future

qMR is becoming a turn-key application

Happy Snappy MRI Camera

transforming into

Scientific Instrument

We are witnessing

paradigm shift

technological revolution

Link: qmri.org/hack2019

- ISMRM special workshop; consensus position paper
- Publish specific medals e.g. T_1, MD (some may already exist)