ON-LINE APPENDIX

To estimate the variance components, a linear mixed model is used separately for each tissue, with fixed effects for subjects, here called individuals (I); MR imaging systems, here called machines (M); sequences (S); and the machines × sequences (MS) interaction. Random effects are all possible interactions with individuals (ie, IM, IS, and IMS). The 3 visits of the individuals are assumed to be pure replications and are nested within the individuals × machines combinations (R:IM). The linear mixed model can be written as

$$Y_{imsr} = \mu + \beta_i + \beta_m + \beta_s + \beta_{ms} + \nu_{im} + \nu_{is} + \nu_{ims} + \nu_{r:im} + \varepsilon_{imsr},$$

where Y_{imsr} is the ADC measurement on individual i on machine m for sequence s at the r-th replication, μ is the intercept, the βs are the fixed effects identified by their indices and, similarly, the νs are the random effects. Finally, the residuals are denoted by ε.

The total variance can be decomposed as

$$\sigma^2_{total} = \sigma^2_{IM} + \sigma^2_{IS} + \sigma^2_{IMS} + \sigma^2_{R:IM} + \sigma^2_{E},$$

where again the variance components are identified by their indices—for example, σ^2_{IS} is the variance of the individuals × sequence random effects. It is possible to estimate sequence-specific residual variances σ^2_{E}, which are denoted by σ^2_{Es}. The models with or without sequence-specific residual variances are compared by using the Akaike Information Criterion.[15]

To compare the measurement precision of the different sequences, the conditional variance, given individual i, machine m, and sequence s,

$$Var(Y_{imsr}|i, m, s) = \sigma^2_{R:IM} + \sigma^2_{Es}$$

is used. The square root is called the standard error of measurement.

The expected value of the difference between new ADC measurements Y_{imsr} and $Y_{ims'r}$ on a new individual i on machine m for sequences s and s' at the same visit is called the bias of sequence s with respect to s'[12]:

$$\text{bias}(s, s') = E(Y_{imsr} - Y_{ims'r} = (\beta_s - \beta_{s'}) + (\beta_{ms} - \beta_{ms'}),$$

and the variance of the difference is

$$Var(Y_{imsr} - Y_{ims'r}) = 2(\sigma^2_{IS} + \sigma^2_{IMS}) + \sigma^2_{Es} + \sigma^2_{Es'}.$$

Combining the 2 expressions yields the 95% limits of agreement between sequences s and s' on the same machine at the same visit:

$$95\%\ \text{LoA}(s, s') = \text{bias}\ (s, s') \pm 1.96 \times \sqrt{Var(Y_{imsr} - Y_{ims'r})} = (\beta_s - \beta_{s'}) + (\beta_{ms} - \beta_{ms'}) \pm 1.96 \times \sqrt{2(\sigma^2_{IS} + \sigma^2_{IMS}) + \sigma^2_{Es} + \sigma^2_{Es'}}$$

The linear mixed model with tissues (T) incorporated as fixed effects can be written as

$$Y_{imstr} = \mu + \beta_i + \beta_m + \beta_s + \beta_t + \beta_{ms} + \beta_{mt} + \beta_{st} + \beta_{mst} + \nu_{im} + \nu_{is} + \nu_{it} + \nu_{ims} + \nu_{imt} + \nu_{ist} + \nu_{imst} + \nu_{r:im} + \nu_{sr:im} + \nu_{tr:im} + \varepsilon_{imstr}.$$

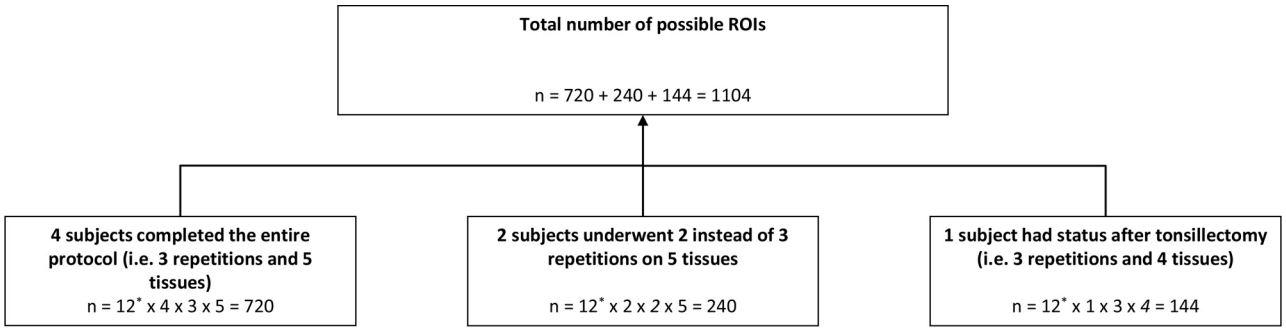
The total variance can be decomposed as

$$\sigma^2_{total} = \sigma^2_{IM} + \sigma^2_{IS} + \sigma^2_{IT} + \sigma^2_{IMS} + \sigma^2_{IMT} + \sigma^2_{IST} + \sigma^2_{IMST} + \sigma^2_{R:IM} + \sigma^2_{SR:IM} + \sigma^2_{TR:IM} + \sigma^2_{Es}$$

and the SEM, defined as the square root of the conditional variance given individual i, machine m, sequence s, and tissue t, is

$$\text{SEM}\ (s) = \sqrt{Var(Y_{imstr}|i,m,s,t)} = \sqrt{\sigma^2_{R:IM} + \sigma^2_{SR:IM} + \sigma^2_{TR:IM} + \sigma^2_{Es}},$$

which may depend on the sequence. For all models, parameter estimates of the fixed effects and variance components are obtained by the method of restricted maximum likelihood by using Proc NLMIXED of SAS (Version 9.2; SAS Institute). Appendix courtesy of D.L. Knol.



*With the 5 used MRI-systems and 3 DWI-sequences the theoretical number of ROIs per system equals (5 x 3 =) 15. However, EPI-DWI-6b was not available on system III and TSE-DWI-2b was not available on system IV and V. Therefore the number of ROIs per system equals (5 x 3 – 3 =) 12 ROIs.

ON-LINE FIG. The total number of possible regions of interest in the current setting, with the 5 MR imaging systems used and 5 selected tissues (submandibular gland, sternocleidomastoid muscle, spinal cord, subdigastric lymph node, and tonsil). Further elimination is due to artifacts or poor image quality.