The Methodology for Accessing the Accuracy of Apparent Diffusion Coefficient Determining

K A Sergunova¹, E S Akhmad¹, D S Semenov¹, A V Petraikin¹, Yu A Vasilev¹, S A Kivasev², N N Potrahov³

¹Research and Practical Center of Medical Radiology, Department of Health Care of Moscow, Moscow, Russia
²Hospital Center JSC «Family Doctor», Moscow, Russia
³Saint Petersburg Electrotechnical University “LETI”, St. Petersburg, Russia

E-mail: ska@rpcmr.org.ru, tel.: 8 (905) 570-15-28

Abstract. One of the criteria for MRI neoplasms assessing is the apparent diffusion coefficient, which is calculated from the diffusion-weighted images. It is a measured parameter and is characterized by some error. A phantom including substances with self-diffusion limited to varying degrees was developed for quality assurance of diffusion-weighted images. The purpose of this work was to develop a methodology for determining the accuracy of methods and controls. The work included identification of errors sources and evaluation of each of them according to the results of numerical and phantom experiments. The method of MR-spectrometry has been used to evaluate the systematic error caused by the phantom control substances. The result of the evaluation of the phantom scan is an estimate of the magnitude of the random error determined by the operation of the tomograph. In addition, the effect of temperature variations on the measurements was evaluated. 11 experiments on tomographs of 5 different manufacturers were conducted. The accuracy of determining the apparent diffusion coefficient by each of them, as well as the comparison of the devices among themselves, showed a 16% variation.

The diffusion coefficient of water molecules in human tissues, which is calculated from the results of diffusion-weighted magnetic resonance imaging (DW-MRI) - the apparent diffusion coefficient (ADC) - is used by radiologists to draw conclusions about the suspicion of a malignant neoplasm. However, currently in the process of MRI technical parameters testing [1], this quantitative indicator is not controlled.

In paper [2], test objects with control substances were proposed for assessing the quality of the parameters of DW-images. To reduce the diffusion coefficient, we used aqueous solutions of polyvinylpyrrolidone (PVP) with concentrations of 0, 10, 20, 30, 40, 50, 60, 70% by weight of the substance. In addition, to simulate the limited movement of water molecules in the intracellular space, reverse emulsions (such as water-in-oil) based on organosilicon compounds (siloxanes) were created.

One of the important tasks in a measurement procedure developing, is the accuracy of the methods and means of control determination. Therefore, the purpose of this work was to estimate the error in ADC measurement in the process of DW-MRI quality control.

The error of the measurements is made up of systematic and random. To identify the magnitude of the systematic error associated with the control substances, the nuclear magnetic resonance method, close to MRI, was chosen as the reference measurement method.

A Bruker AVANCE 600 MR spectrometer was used to perform a series of measurements using a 2D DOSY method based on a stimulated spin-echo pulse sequence with bipolar gradient magnetic field pulses and a time delay used to compensate for the influence of Foucault currents (STE-LED). The amplitude values of the gradients (G) ranged from 2.5 to 50 Gs / cm. The total error of the results obtained was determined according to equation (1), based on the instrumental error of the MR-spectrometer (Δspec, D) and of the software (σapp), as well as the error of the influencing value - the temperature of the control substance and the environment (Δspec, T).
\[ \Delta_{\text{spec}} = \sqrt{\Delta_{\text{spec,}T}^2 + \sigma_{\text{app}}^2 + \left( t_{P,\infty} \cdot \frac{1}{3} \Delta_{\text{spec,}D} \right)^2}, \]  

where \( t_{P,\infty} \) – Student’s coefficient determined on the basis of the selected significance level \( P \) and the number of measurements \( n = \infty \).

The instrumental error associated with the accuracy of the signal intensity recording was calculated as follows:

\[ \Delta_{\text{spec,}D} = f'(I) \Delta I = \frac{\Delta I}{IG^2 \gamma^2 \delta^2 (\Delta - \frac{\delta}{3}) \cdot 10^4}, \]

where \( \gamma \) – gyromagnetic ratio; 
\( \delta \) – gradient pulse duration; 
\( \Delta \) – distance between gradient pulses, 
\( \Delta I = 0.003*1 \) (for Bruker AVANCE 600 the limits of the permissible relative error in recording the signal intensity for the peak of the spectral curves are ± 0.3\%)

To calculate the approximation error, the number of indirect measurements was taken into account \( n \):

\[ \sigma_{\text{app}} = \sqrt{\frac{\sum_{i=1}^{n} (D_i - \hat{D}_i)^2}{n(n-1)}}, \]

where \( D_i \) – calculated diffusion coefficient values; 
\( \hat{D}_i \) – values of the function approximation at \( i \) point.

For 40\% PVP instrument errors and approximations were 2.59\*10^{-11} m²/s and 3.47\*10^{-11} m²/s respectively.

The influence of the instrument temperature setting accuracy was also evaluated in the determination of the diffusion coefficient measurement error in an MR spectrometer. As a result of experimental studies (Fig. 1), it was confirmed that in the temperature range from 20°C to 30°C, the diffusion coefficient of water molecules is approximated by the formula (4) [3] with the coefficient of determination \( R^2 = 0.996 \):

\[ D = D_0 \left( \frac{T}{T_s} - 1 \right)^\alpha, \]

where \( D_0, T_s \) and \( \alpha \) – approximation coefficients.

The temperature contribution on diffusion coefficient measurement was determined by differentiating of (4):

\[ \Delta_{\text{spec}} = \frac{\Delta T \alpha D_0}{T_s} \left( \frac{T}{T_s} - 1 \right)^{\alpha-1}. \]

For 40\% PVP it was: \( \Delta_{\text{spec,}T} = 4.11\*10^{-12} \) m²/s.
Thus, the measured on an MR spectrometer diffusion coefficient for 40% PVP was $1.23 \times 10^{-9}$ m$^2$/s at 30°C, and the total absolute measurement error was $\Delta_{\text{spec}} = 4.35 \times 10^{-11}$ m$^2$/s, which in relative terms is 3.5% at a significance level of 0.95.

After assessing the error due to control substances, a statistical analysis of the data obtained by MRI was performed. The procedure for assessing the error of measurement of the diffusion coefficient in MRI consisted of the following steps:
- registration of the MR image in the DW-MRI mode and the construction of ADC maps;
- selection of the region of interest on the ADC map for control substances and drawing up samples of pixels inside it;
- the calculation of the average value (according to the formula 6) and the standard deviation (according to the formula 7) for each sample of pixels;

$$\bar{D} = \frac{\sum_{i=1}^{n} D_i}{n},$$  \hspace{1cm} (6)

$$\sigma = \sqrt{\frac{\sum_{i=1}^{n} (D_i - \bar{D})^2}{n-1}},$$  \hspace{1cm} (7)

where $D_i$ – ADC value for $i$-th pixel, and $n$ – total number of pixels in the sample.

- gross errors in the sample search – filtering values that are not included in the interval $D_i \notin (\bar{D} - 3\sigma, \bar{D} + 3\sigma)$;

- recalculation for the final sample of the mean and standard deviation (6-7);
- verification of compliance of the pixel intensity distribution with the normal distribution;
- calculation of the confidence interval: $\Delta_{\text{MRI}} = t_{p,\alpha} \sigma / n$. 

**Figure 1.** The apparent diffusion coefficient of water and temperature dependency diagram
Figure 2. An example of ADC-map processing. a) ADC-map of phantom with control substances, showing the elliptical region of interest in the area of the test tube with water; b) histogram of the distribution of diffusion coefficient values.

To control the ADC measurement error in the DW-MRI, a series of measurements were taken on tomographs of different manufacturers (Siemens, Philips, Toshiba, General Electric, Hitachi). The total number of tests performed was 11. By statistical evaluation of the measured values, a comparison was made between the mean value and the half-width of the confidence interval.

Thus, the measured on an MR spectrometer diffusion coefficient for 40% PVP was $1.23 \times 10^{-9} \text{m}^2/\text{s}$ at 30°C, and the total absolute measurement error $\Delta_{\text{spec}} = 4.35 \times 10^{-11} \text{m}^2/\text{s}$, which in relative terms is equal to 3.5% at a significance level of 0.95.

ADC differences between models amounted to 16%. The magnitude of the random error of the measurements, for example, on an MRI of the company "Hitachi" for PVP 40% equals to $0.03 \times 10^{-12} \text{m}^2/\text{s}$. The scatter of the half-width of the confidence interval when comparing the results on all tomographs is (from 4 to 33) $\times 10^{-12} \text{m}^2/\text{s}$ for b-factor equal to 600 s/mm².

In this paper, an assessment of factors affecting the diffusion coefficient measurement error is carried out, theoretical calculations of the calculation and quantitative assessment are given on the example of one control substance.

References
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