

MRI DIFFUSION WEIGHTED IMAGING

Lab protocol for the module “Bioimaging”

Group one practical two



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Introduction and Theory

Radiology intends to image organisms with non-invasive imaging techniques. One of the methods used is Magnetic resonance Imaging (MRI). Here, the human/specimen is imaged using the alignment of nuclear spins in protons. Different measuring techniques like changing parameters or varying sequences influence the contrast. Depending on the examined area and research question a wide variety of measuring techniques can be chosen to reach the best image for this cause.

MRI can not only image stationary tissue but also diffusion (movement of water in biological tissue). This can be achieved by using Diffusion weighted Imaging (DWI). To achieve DWI field gradients, radiofrequency (RF) pulses and timing parameters are used. Generally, spin-echo (SE) or echo-planar imaging (EPI) sequences are used. The RF pulses used are 90° and 180° pulses which are the standard for spin-echo sequences and good for preserving the signal in DWI. To achieve DWI field gradients are added to a spin-echo sequence in pairs to create a signal attenuation correlating with the degree of diffusion. The first gradient (dephasing) after the 90° RF pulse induces a phase shift depending on the position of the spins. The second gradient (rephasing) is applied after the 180° RF pulse and reverses the phase shift for stationary spins. Therefore, only the phase shift of moving spins is left. The net phase shift for diffusing water molecules results in signal loss.

The b-value describes the effect of the diffusion gradients quantitatively and is influenced by the gradient strength (G), the gradient duration (δ) and the time difference between pulses (Δ). It can be calculated by the following equation: $b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$.

For fast image acquisition in emergency cases EPI is used. RF pulses and diffusion gradients are applied as mentioned above. The necessary k-space data is acquired in one shot using a series of frequency-encoding gradients. Like this, motion artifacts can be minimized, and patient comfort is improved due to the shorter acquisition time.

Timing is a critical factor in DWI. The echo time (TE) needs to be long enough to accommodate the diffusion gradients while allowing the spin echo to form. Meanwhile the repetition time (TR) influences the overall scanning time and must balance the signal-to-noise ratio (SNR) and tissue relaxation effects. TE and TR need to be synchronized to the RF pulses to visualize the diffusion effects.

Diffusion gradients are applied in different directions to visualize multi-directional diffusion. Single direction DWI is used for basic applications like stroke imaging while multi-directional imaging is used for characterizing anisotropy. Here, gradients are applied in at least 6 non-collinear directions. More complex models use up to 12 directions.

The directional dependence can be calculated using the Apparent Diffusion Coefficient (ADC) which the following equation:

$$ADC = \frac{\ln(S0/S)}{b_1 - b_0}.$$

Low ADC values indicated a restricted diffusion while high ADC values indicate free diffusion. The unit of the ADC is $[\text{mm}^2/\text{s}]$.

A second parameter is used describe DWI. The Fractional Anisotropy (FA) characterised the orientation of the diffusion within the tissue. The FA ranges from 0 to 1, whereas higher values calculated are caused by greater anisotropy or more restricted diffusion. It can be calculated by the following equation:

$$FA = \sqrt{\frac{3 \sum_{1,2,3} (\lambda_i - \bar{\lambda})^2}{2 \sum_{1,2,3} \lambda_i^2}}$$

Experiments

The following three experiments were performed to visualize diffusion in different spatial conditions. Both an isotropic and an anisotropic model were imaged as well as a healthy test subject in different gradient directions.

1st experiment: isotropic test object

A spherical phantom was used to simulate an isotropic object. A spin-echo sequence was performed to select the central coronal slice. Then a measurement with EPI was performed in the selected slice (1) which was then adjusted by changing 2. field of view (FOV), 3. less phase encoding steps, shorter acquisition time, bigger voxels, 4. Smaller echo spacing and reduced TE, and 5. Increased signal intensity. Then the b-values were changed (0,100,200,300,400,500,600,700,800,900,1000) and the TR was increased to 1000ms to calculate the ADC later. Lastly, the measurement was performed in three different directions to verify the independence of the signal drop of the field gradients.

2nd experiment: non-isotropic object

A leek in a Tupperware container was used to simulate a non-isotropic object. The measurements include a localizer, slice selection, and b value variations (0,100,200,300,400,500,600,700,800,900,1000 in three directions) measurements.

3rd experiment on a healthy subject

A healthy volunteer's brain was scanned last to include some in vivo measurements. A localizer and slice selection spin-echo were performed. The same sequences as for experiment 2 were acquired for 11 different b-values in three directions.

Evaluation

1st experiment: isotropic test object

The central coronal slice was selected and the FOV and TE were adjusted as described earlier to achieve the best possible resolution. These parameters were set for the next experiments.

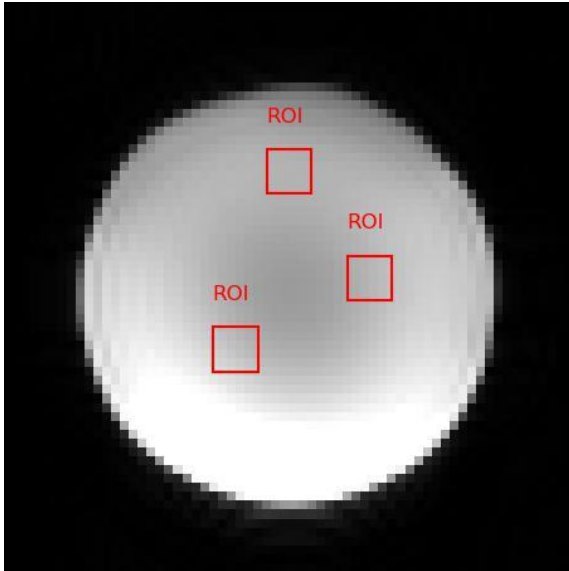


Figure 1 Image of the phantom sphere with 3 ROIs in red at $b=0$. With ROI 1 on the top, ROI 2 on the right and ROI 3 on the left

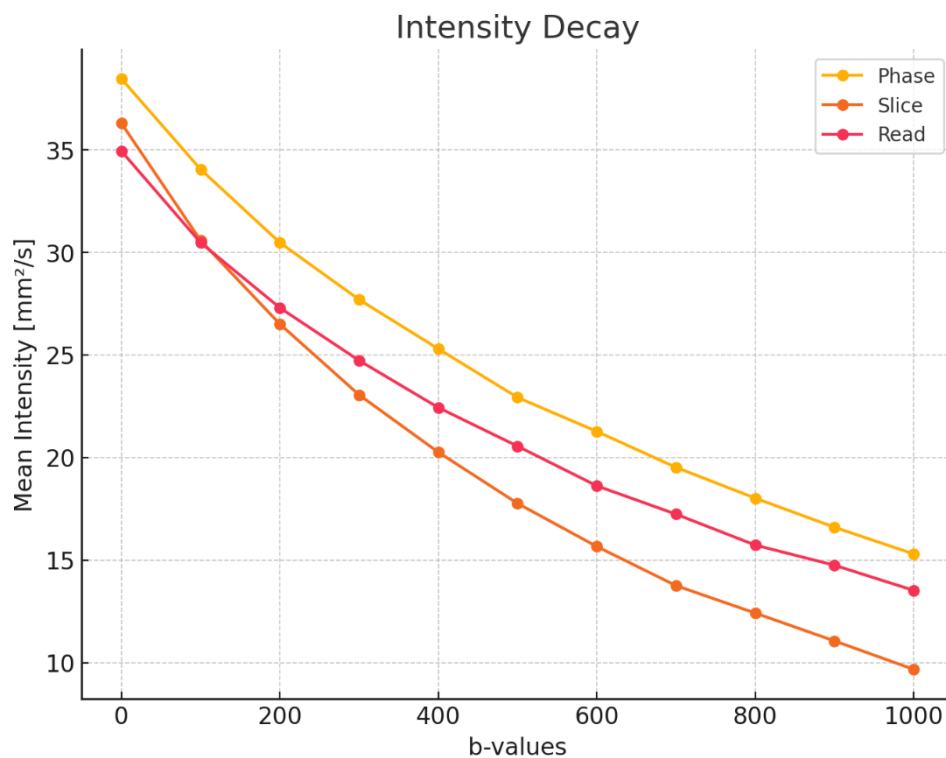


Figure 2 Plot of the mean intensity vs the b -value of 3 different slice encoding sequences. ROI 1 used for calculating the intensities. The mean intensity values were divided by 100 for better visualization

Several acquisitions were made in slice, phase and read direction with b -values ranging from 0 to 1000 in 100 value steps. Three ROI were defined Figure 1 Image of the phantom sphere with 3 ROIs

in red at $b=0$. With ROI 1 on the top, ROI 2 on the right and ROI 3 on the left as visible in Figure 1. In Figure 2 the mean intensity is plotted against the b -values of the different acquisitions. It becomes visible that the decay with a logarithmic scaled y-axis is nearly linear.

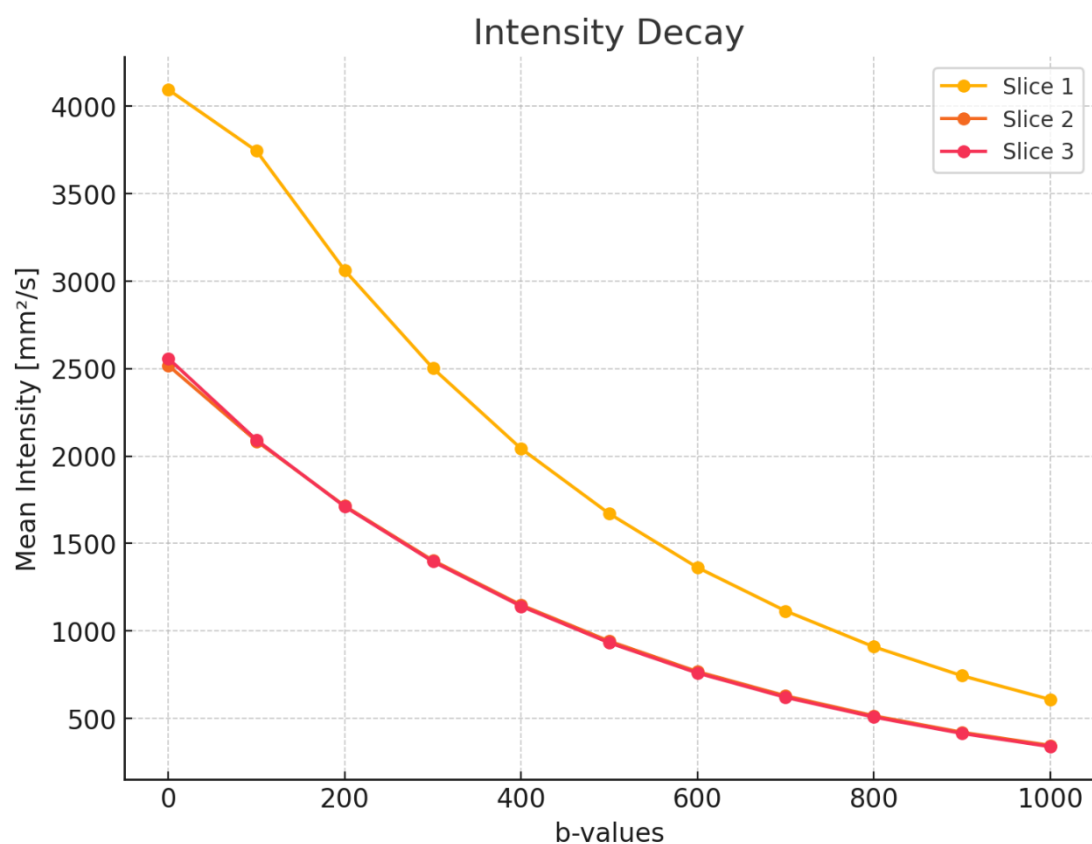


Figure 3 Mean intensity vs b value of 3 different ROI in slice phase encoding direction

In Figure 3 it becomes visible that the b -values decay at a around linear rate (logarithmic y-axis) when comparing the different ROIs from the same phase encoding direction. ROI 2 and 3 are also around the same brightness which can be verified by the optical image. In contrast to that ROI 1 is the brightest which is also reflected in the higher mean intensity in Figure 3.

Table 1 ADC calculation of the sphere phantom with three ROI. Read 1 equals a measurement in read direction and the first ROI

	Read 1	Read 2	Read 3	Phase 1	Phase 2	Phase 3	Slice 1	Slice 2	Slice 3
ADC (all) [mm ² /s]	0.0018 5938	0.0020 0187	0.0019 6891	0.0019 4186	0.0020 0586	0.0020 3666	0.0019 0683	0.0019 8642	0.0020 2290
ADC (low) [mm ² /s]	0.0019 7409	0.0020 0568	0.0019 7494	0.0020 4682	0.0020 1422	0.0020 3787	0.0020 1771	0.0019 8773	0.0020 2085
ADC (high) [mm ² /s]	0.0019 8943	0.0020 0143	0.0019 8831	0.0020 3515	0.0020 1548	0.0020 3787	0.0020 1666	0.0019 9627	0.0020 2024

The ADCs seen in table 1 were calculated with the Formula mentioned earlier. The range is quite narrow between 0.0018 [mm²/s] to 0.00202290 [mm²/s]. This can be explained by the isotropic diffusion properties of the spherical phantom. Also the total ADC is quite similar to the ADC (low) and ADC(high) also indication free diffusion within the sphere.

2nd experiment: non-isotropic object

In the second experiment the influence of the encoding directions was of interest. Here, a leek was testing subject, which is why the ROI was placed inside the leek and imaged with the same parameters as the experiment before. Figure 4 shows that the decay of the mean intensity of the ROI inside the leek (see Figure 5) is almost linear but not as similar as in experiment 1 Figure 2.

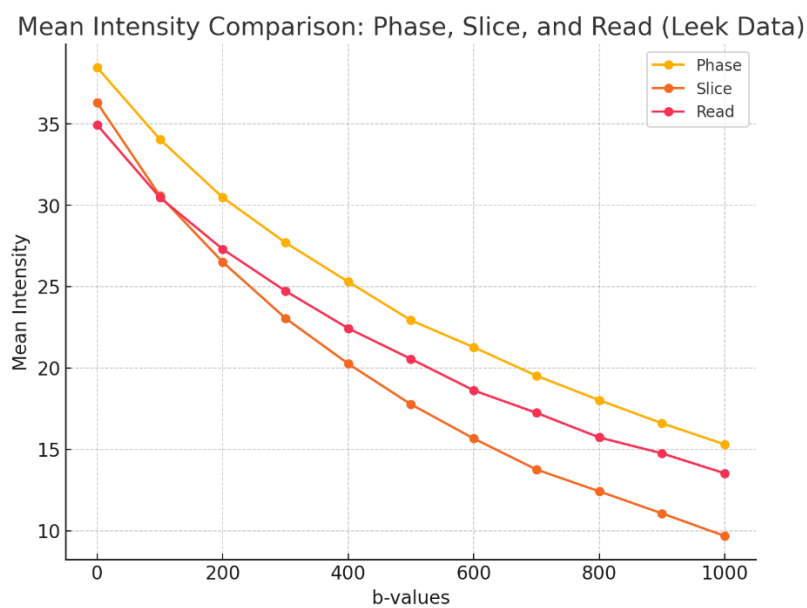


Figure 4 plot of the mean intensity measured (divided by 100) for the ROI plotted against the b-values

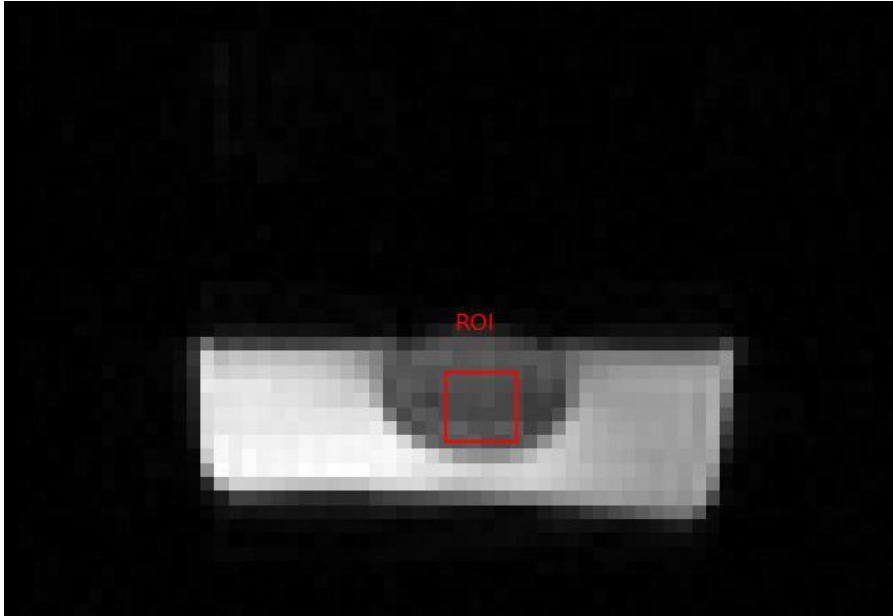


Figure 5 Image of the leek with ROI inside at rear direction with a b-value of 0

Table 2 ADC values calculated for the ROI inside the leek

ADC	read	phase	slice
ADC(all) [mm ² /s]	0.00094838	0.00092126	0.00132128
ADC(low) [mm ² /s]	0.00098384	0.00098786	0.00135685
ADC(high) [mm ² /s]	0.00079876	0.00082318	0.00120369

The ADC values calculated in Table 2 show that there is a difference between the encoding directions. The read and phase directions show similar ADC values which is still lower than the value calculated for water earlier (~ 0.0020 [mm²/s]). This is also confirmed by the optical image, since the water around the leek also shows a different shade of grey than the leek in read and phase direction. The ADC values for the slice direction are higher and not matching the values from the other directions. This can be explained by the alignment of the leek fibres with the slice sequence. Since the values are still quite close to the values measured for water, it can be assumed that there is diffusion restriction within the leek in read and phase direction while the diffusion is less restricted in slice direction. A drop in ADC values at high b-values can be observed in read and phase direction which can also be an indicator of restricted diffusion. This is caused by the scan being more sensitive to restricted diffusion at higher b-values.

3rd experiment: healthy subject

In the 3rd experiment healthy volunteers' brain was measured. 4 ROIs were placed into different sections of the brain to compare ADC values and therefore diffusion rates.

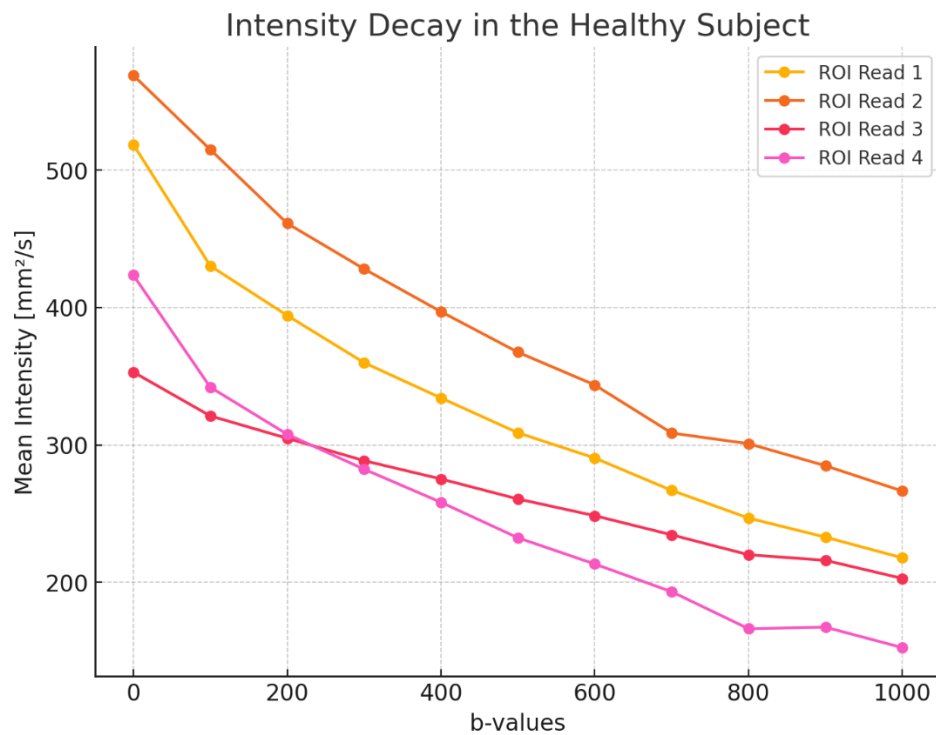


Figure 6 Intensity Decay of the mean intensity vs the b-values in the healthy brain measured

In Figure 6 it becomes visible that the intensity decay is more irregular in the brain than in the previous experiments. The Signal decays less linearly (with log scale in y-axis) since the material scanned now is not only water but complex brain tissue. Therefore, in the direct comparison a different decay can be explained by the change in material.

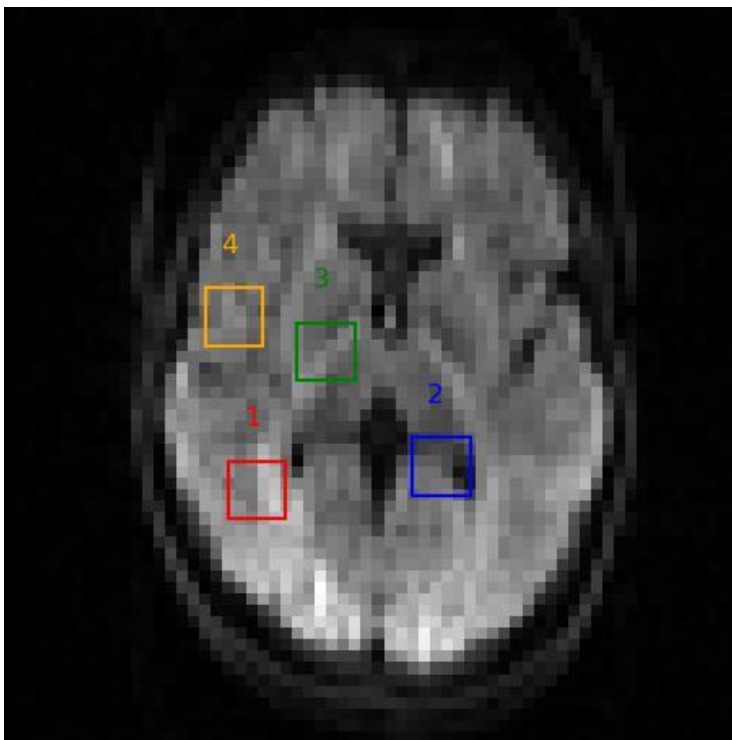


Figure 7 ROI placement on an MRI scan of a healthy brain

Table 3 ADC values for 4 different ROI in the brain. All values in mm²/s

ADC [mm ² /s] ADC (all)	ROI 1			ROI 2		
	read	phase	slice	read	phase	slice
	0.00086795	0.00120505	0.00114601	0.00075909	0.00092112	0.00069220
ADC (low)	0.00082981	0.00137651	0.00109856	0.00084391	0.00106878	0.00076823
ADC (high)	0.00072010	0.00084296	0.00085937	0.00063661	0.00082238	0.00057218
ADC (all)	ROI 3			ROI 4		
	read	phase	slice	read	phase	slice
	0.00055449	0.00083717	0.00088135	0.00102236	0.001006	0.00077807
ADC (low)	0.00052187	0.00081979	0.00094431	0.00096615	0.00105239	0.00083238
ADC (high)	0.00050804	0.00073689	0.00072930	0.00084030	0.00085912	0.00066903

In Table 3 the ADCs are listed. For ROI 1 it is visible that the ADC value for the read direction is lower indicating restricted diffusion in this direction and therefore denser structures like white matter. The placement of the ROI in the optical images (figure 7) supports this hypothesis. The significant drop of the ADC values at higher b values in phase direction also suggests this. ROI 2 has even lower ADC values across all encoding directions suggesting restricted diffusion. The placement in the optical images supports this assumption. The drop of the ADC value at higher b-value is still visible but less drastic as at the previous ROI. ROI 3 similar ADC values in phase and slice direction and even lower ADC values in read direction. This suggests that there is more diffusion in phase and slice direction than in read direction. The absolute values are still quite low suggesting low diffusion rates overall. The mean intensity values (see appendix) are homogeneous which suggests a homogeneous brain structure within this ROI in all directions. This might also explain why no high ADC values can be observed even though the liquor is part of this ROI and should exhibit high ADCs. ROI 4 shows the highest ADC value in read direction and the lowest ADC value in slice direction. The read and phase directions show the highest diffusion rate while the slice direction is rather restricted in its diffusion. The low ADC values suggest a nerve fibre in this direction since nerve fibres restrict diffusion. The significant drop in ADC values at high b values also supports this assumption.

Table 4 ADC map values compared to measured ADC values in comparable ROIs

ADC [mm ² /s]*10 ⁻³	ADC map	ADC map	measured data	
	phase	slice	phase	slice
ROI 1	866.8125	660.375	1205.04667	1146.00697
ROI 2	971.25	810.125	921.122983	692.195615
ROI 3	844.3125	860.5625	837.166183	881.345485
ROI 4	1109.4375	1043.875	1006.27592	778.069294

The ADC values measured were compared to an ADC map computed by the scanner. ROI shows quite different ADC values and therefore different conclusions about the diffusion in this spot. ROI2 shows similar data in the phase direction and different data in the slice direction indicating a nerve fibre running in slice direction in the measured data. For ROI 3 the data in both directions looks quite similar and therefore restricted diffusion in this ROI. ROI 4 shows similar values in the phase direction and lower measured ADC than in the ADC map.

The difference in the ADC maps could be due to the ROIs placement. The placement of the ROI was close but probably not exactly the same (see images in the appendix). Since the mean intensity does not reflect on the inhomogeneity of an area, a slightly different ROI placement can affect the ADC vastly. Even when choosing the same coordinates of the ROI the placement can be different due to variations in anatomy.

Discussion

1st experiment sphere phantom

The ADC values measured in the first experiment match the values expected for water suggesting that the measurement and calculation was successful. The decay follows approximately a linear decay as was expected. ROIs with a similar brightness show similar mean intensities. There was no difference observed in varying phase encoding directions. Low ADC and high ADC are also approximately the same as the overall ADC. This matches the expectation of the properties of a water filled phantom since the diffusion is not restricted here.

2nd experiment leek phantom

The mean intensities measured decay linearly (with log scale in y-axis) as well, but the values differ a little more than the water phantom. Overall, the plot still looks similar to the sphere phantom. The ADC values are varying depending on the phase encoding direction. The fibres of leek are aligned with the slice direction which is reflected by the ADC values. Even better representation could be reached by better imaging quality to place the ROI better since the Image currently has quite a large voxel size. Along the leek fibres the diffusion is less restricted than in phase and read direction. This can be confirmed by the higher ADC values for the slice direction. The drop in ADC values at higher b-values also supports this hypothesis.

3rd healthy subject

The four ROIs were placed in different regions of the brain to measure their diffusion properties. For example, ROI 2 was placed at the liquor and should therefore have a similar ADC to water since diffusion is rather unrestricted in this area. This could not be confirmed. The other ROIs showed ADC values closer to the expected data for this brain region but was still not as close to the ADC map data as one would hope for. So, the trend of the ADC values calculated is generally right, but the absolute values do not match precisely.

For future data processing a smaller ROI size could solve this issue since the tissue measure will be less heterogeneous and therefore the values more accurate. Raw images with a higher resolution could also benefit ROI placement since brain regions can hardly be identified with the current resolution. Since the ADC values can provide information about nerve fibres and their directions, properly identifying the brain anatomy is crucial for an insightful interpretation of the ADC values.

Furthermore, the analysis of multiple smaller ROIs close to each other could give insight into the exact localization of nerve fibres and membranes inside the brain. To achieve this the python algorithm to calculate the mean intensities and ADCs needs to be adjusted further so fewer manual steps are needed. Then bigger datasets can be processed faster and will lead to better insights.

Appendix

<i>b</i>	read 1 [mm²/ s]	read 2[mm² /s]	read 3	phase 1 [mm²/s]	phase 2 [mm²/ s]	phas e 3 [mm² /s]	slice 1 [mm²/s]	slice 2 [mm²/s]	slice 3 [mm²/ s]
0.000 0	4095.0 000	2688.6 250	2575. 9375	4093.687 5	2511.2 500	2770. 8750	4095.000 0	2517.562 5	2558.1 875
100.0 000	3803.7 500	2206.6 250	2149. 5000	3691.250 0	2083.9 375	2264. 8750	3744.750 0	2085.500 0	2092.0 000
200.0 000	3133.9 375	1806.8 750	1770. 3125	3008.000 0	1708.2 500	1849. 7500	3062.000 0	1714.937 5	1710.6 250
300.0 000	2568.8 125	1479.6 250	1449. 0000	2449.187 5	1394.1 250	1507. 3125	2502.250 0	1403.312 5	1396.8 125
400.0 000	2104.5 000	1209.4 375	1186. 8125	1996.500 0	1137.2 500	1229. 0000	2042.687 5	1148.437 5	1141.3 750
500.0 000	1726.9 375	989.25 00	975.5 625	1627.812 5	931.06 25	1002. 3750	1670.750 0	941.6875	932.18 75
600.0 000	1413.6 250	808.75 00	796.6 250	1325.312 5	756.62 50	816.8 125	1362.875 0	767.5000	759.18 75
700.0 000	1158.8 750	661.75 00	654.8 125	1080.562 5	619.31 25	665.6 250	1114.437 5	628.9375	620.18 75
800.0 000	950.75 00	540.18 75	535.7 500	881.0625	505.87 50	542.6 875	909.4375	514.8750	507.56 25
900.0 000	779.50 00	443.25 00	437.7 500	717.8750	412.00 00	442.7 500	744.0000	420.3750	413.75 00

1000.	637.87	363.18	359.6	587.1875	337.87	361.5	608.3125	345.3750	338.37
0000	50	75	250		50	000			50

Raw values for the first experiment (sphere measurements)

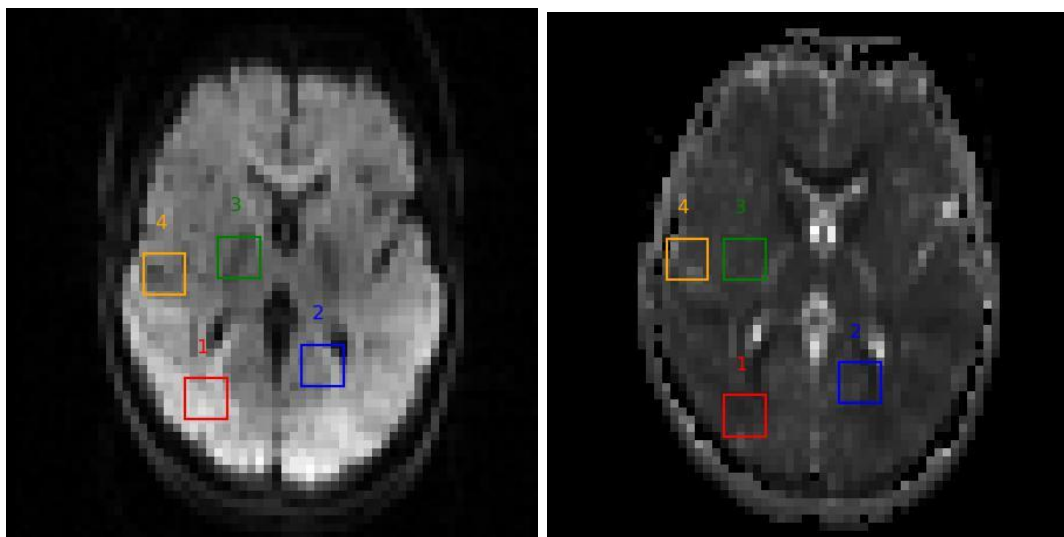
<i>b</i>	Read [mm ² /s]	Phase [mm ² /s]	Slice [mm ² /s]
0	34.93125000	38.45625000	36.28750000
100	30.46875000	34.04375000	30.57500000
200	27.30000000	30.47500000	26.50625000
300	24.73125000	27.70000000	23.05625000
400	22.43750000	25.30000000	20.26250000
500	20.55625000	22.93125000	17.76875000
600	18.62500000	21.27500000	15.66875000
700	17.24375000	19.52500000	13.76250000
800	15.73750000	18.02500000	12.42500000
900	14.75625000	16.60625000	11.06875000
1000	13.53125000	15.30625000	9.68125000

Raw values for experiment 2 (leek)

<i>b</i>	ROI read 1 [mm ² / s]	ROI read 2 [mm ² / s]	ROI read 3 [mm ² / s]	ROI read 4 [mm ² / s]	ROI phase 1 [mm ² /s]	ROI phase 2 [mm ² /s]	ROI phase 3 [mm ² /s]	ROI phase 4 [mm ² /s]	ROI slic e 1 [m m ² /s]	ROI slic e 2 [m m ² /s]	slic e ROI 3 [m m ² /s]	ROI slic e 4 [m m ² /s]
0.0 00 0	518.6 875	569.0 625	353.0 000	423.5 625	543.5 000	628.8 125	345.7 500	4477 5.000 0	56 1.6 87 5	65 6.5 00 0	35 4.1 25 0	45 3.6 87 5
10 0.0 00 0	430.3 750	515.0 625	321.1 250	342.0 000	424.6 875	550.3 125	306.9 375	3801 875.0 000	43 8.0 00 0	58 4.6 87 5	31 5.5 00 0	40 0.5 62 5
20 0.0 00 0	394.2 500	461.3 125	304.8 125	307.7 500	345.5 000	496.1 875	281.1 875	3337 5.000 0	37 5.1 25 0	54 3.1 25 0	28 2.4 37 5	36 2.8 12 5
30 0.0 00 0	359.8 750	428.1 250	288.5 000	282.3 125	321.1 875	445.4 375	255.7 500	3037 5.000 0	33 7.1 25 0	51 1.8 12 5	25 8.7 50 0	33 5.2 50 0
40 0.0 00 0	334.1 875	397.0 000	275.1 875	258.1 875	276.4 375	399.3 750	239.3 750	2765. 0000	30 6.1 87 5	47 5.6 25 0	23 7.0 00 0	30 9.8 12 5

50	308.8	367.5	260.6	232.3	244.8	358.8	221.1	2495	28	43	21	28
0.0	125	000	250	750	750	750	250	625.0	2.2	0.0	6.2	7.1
00								000	50	00	50	25
0									0	0	0	0
60	290.4	343.6	248.4	213.2	228.1	347.8	201.0	2308	25	41	19	27
0.0	375	250	375	500	875	125	000	125.0	1.8	3.0	6.3	2.3
00								000	12	62	75	12
0									5	5	0	5
70	266.8	308.6	234.5	193.0	211.0	321.0	184.8	2091	22	38	18	26
0.0	750	250	000	625	625	625	125	875.0	7.0	1.8	2.8	4.6
00								000	00	75	75	87
0									0	0	0	5
80	246.6	300.8	220.0	166.1	188.0	279.6	172.4	1928	21	35	17	23
0.0	875	750	000	250	000	875	375	75.00	3.5	5.8	0.3	8.3
00								00	00	12	12	75
0									0	5	5	0
90	232.8	284.8	215.9	167.2	174.6	267.3	161.3	1765.	19	34	15	22
0.0	125	125	375	500	875	125	125	0000	4.3	3.2	7.0	3.4
00									75	50	00	37
0									0	0	0	5
10	217.7	266.3	202.7	152.3	162.8	250.3	149.6	1636	17	32	14	20
00.	500	750	500	750	750	125	875	875.0	8.5	8.5	6.6	8.3
00								000	62	62	87	75
00									5	5	5	0

Raw data of the brain measurements



Measured brain on the left and ADC map on the right