

REPRODUCIBILITY OF LEUKOARAIOSIS SEGMENTATION ON FLAIR SEQUENCE MAGNETIC RESONANCE SCANS

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Abstract

Introduction: Leukoaraiosis is a disease of the cerebral white matter in aged individuals. It shows up as an increased signal intensity on Flair sequences performed as part of magnetic resonance (MR) brain scans. Although the Flair sequence is the commonly used sequence for leukoaraiosis segmentation, it still seems to be a subjective method.

Aim: The aim of the study was to investigate the inter-observer reproducibility of semi-automatic segmentation of leukoaraiosis on Flair sequenced MR scans.

Materials and Methods: 10 MR brain scans were analyzed with the software “Segmentation Leukoaraiose Adelaide” from the IADI laboratory performed by two observers parallelly. The segmentation carried out by the two observer were compared and statistically analyzed.

Results: There was a statistically significant difference ($p < 0,05$) between the leukoaraiosis segmentation performed by the two observer.

Conclusion: The leukoaraiosis segmentation on Flair sequenced MR scans seems to be not reproducible. Thus we have to find parameters more sensitive, reproducible and efficient in order to assess and predict brain aging. Other sequences, like diffusion tensor imaging (DTI), seems to be promising, but needs further evaluation for its utilization in a clinical practice.

Key words: leukoaraiosis, segmentation, MRI, Flair

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1 Introduction

As people age, there are numerous changes that take place, whether physical, chemical or biological. Therefore, it is logical to assume, the brain is no exception to this phenomenon. Neurons are dying every day, the number of synapses decreases and neurons lose the ability to change their structure and function. So far, MRI is the best imaging technique to assess these changes. Among brain aging abnormalities observed on MRI, *leukoariosis* is an often described abnormality, found in the literature, as well as in the clinical practice.

1.1 Leukoariosis

In 1986 neurologists were found a type of tissue change on computerized tomography (CT) and magnetic resonance imaging (MRI) of the brain for which no fitting term existed.[1][2] To avoid confusing an imaging appearance with a specific pathology, neurologists have introduced the term *leukoariosis*. The Greek root *leuko*, signifies "white", and *ariosis* "rarefaction, diminution of density". The leukoariosis is thus a descriptive term for rarefaction of the white matter of the central nervous system.

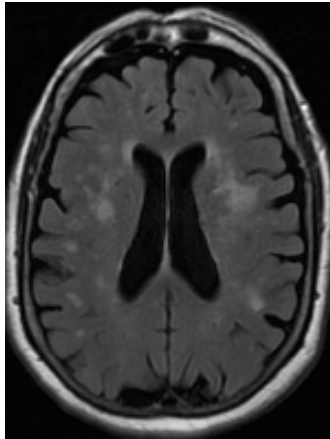


Figure 1.1: Leukoariosis on an MR image

The leukoariosis shows up as decreased density on CT and increased signal intensity on T2/FLAIR sequences performed as part of MRI brain scans. This white matter abnormality occurs diffusely in the brain. It begins in the perivascular area and spreads to the paraventricular region,

to the basal ganglia, sometimes even to the brain stem and it grows in size with the age.

Neurologists often come across this appearance, but its significance is sometimes uncertain and its effects on cognitive function are unclear.[3] Many patients can have leukoaraiosis without any associated clinical abnormality. However, underlying vascular mechanisms are suspected to be the cause of the imaging findings.[4] Hypertension, smoking, diabetes, hyperhomocysteinemia, and heart disease are all risk factors for leukoaraiosis. The abnormalities are thought to be caused by multiple small vessel infarcts in the sub cortical white matter, often the result of chronic hypertension leading to lipohyalinosis of the small vessels.

Since leukoaraiosis is mostly studied and the most visible on the MR images, a further description of the MRI follows.

1.2 MRI

Magnetic resonance imaging (MRI) is a medical imaging technique used in radiology to visualize internal structures of the body. It provides good contrast between the different soft tissues of the body, which makes it especially useful in imaging the brain, muscles, the heart. In clinical practice, MRI is used to distinguish pathological tissue (such as a brain tumor) from normal tissue. One advantage of an MRI scan is that it is harmless to the patient, unlike CT scans and traditional X-rays, which both use ionizing radiation. While CT provides good spatial resolution, MRI provides comparable resolution with far better contrast resolution (the ability to distinguish the differences between two similar but not identical tissues).

The basis of MRI lies in the nuclear magnetic resonance (NMR). NMR is a physical phenomenon in which magnetic nuclei in a magnetic field absorb and re-emit electromagnetic radiation. The emitted energy has a specific resonance frequency which depends on the strength of the magnetic field and the magnetic properties of the isotope of the atoms and which can be detected by a conductive field coil. Nuclei containing an odd number of protons and neutrons have a characteristic motion which is used to detect them. Hydrogen atom is one of those particles, and since it is very abundant in the human body it is adequate for the MR image acquisition.

To obtain an MR image of an object, the object is placed in a uniform magnetic field, B_0 . As a result, the object's hydrogen nuclei align with the magnetic field and create a net magnetic moment, M , parallel to B_0 . This behavior is illustrated in Figure 1.2.

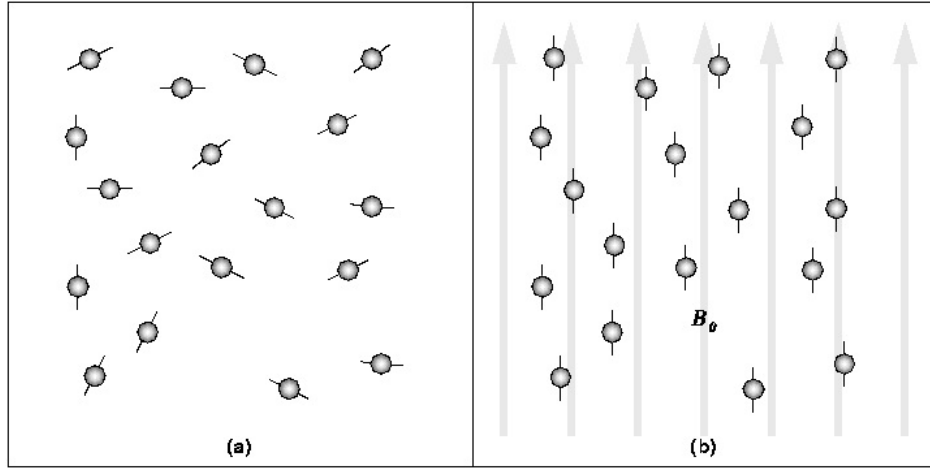


Figure 1.2: In the absence of a strong magnetic field, hydrogen nuclei are randomly aligned as in (a). When the strong magnetic field, B_0 , is applied, the hydrogen nuclei spin at the direction of the field as in (b).

Next, a radio-frequency (RF) pulse, B_{rf} , is applied perpendicular to B_0 . This pulse, with a frequency specific for the nuclei, causes M to turn away from B_0 as in Figure 1.3a.

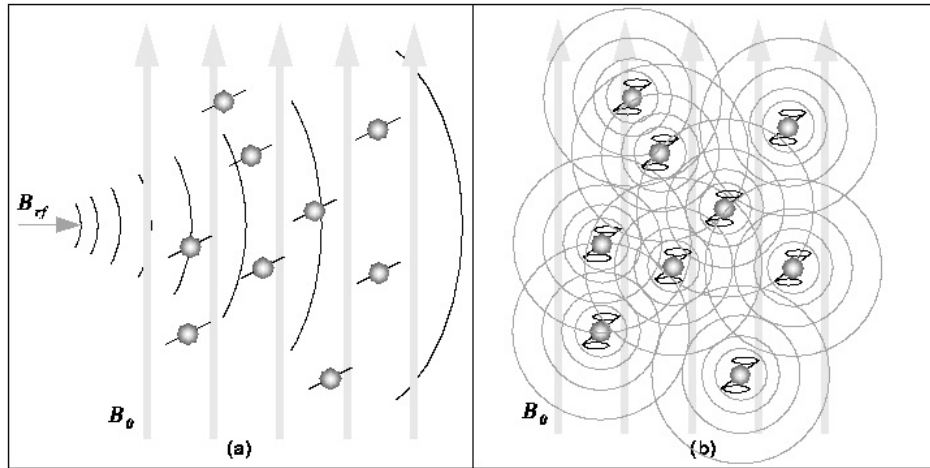


Figure 1.3: The RF pulse, B_{rf} , causes the net magnetic moment of the nuclei, M , to turn away from B_0 (a). When the RF pulse stops, the nuclei return to equilibrium such that M is again parallel to B_0 . During realignment, the nuclei lose energy and a measurable RF signal (b).

Once the RF signal is removed, the nuclei realign themselves such that their net magnetic moment, M , is again parallel with B_0 . This return to equilibrium is referred to as *relaxation*. During relaxation, the nuclei lose energy by emitting their own RF signal. This signal is measured by a conductive field coil placed around the object being imaged. This measurement is processed or *reconstructed* to obtain 3D grey-scale MR images.

For the spatial encoding of the emitted signal, an other magnet is introduced to the system. This magnet is called the *gradient*. With an ordered combination of RF and gradient pulses various data can be acquired to form the image. This leads to different types of MR image acquisitions called *sequences*. There are over a hundred different sequences.

One of those sequences is the Fluid Attenuated Inversion Recovery (FLAIR) sequence. It is a sequence like T2, but there is a null signal from fluids. It can be used therefore in brain imaging e.g. to suppress cerebrospinal fluid.

The evaluation of leukoaraiosis on the FLAIR sequenced MR images is mostly performed subjectively in clinical practice and semi-quantitatively in studies with visual scales like the Fazekas scale.[5][6] This scale consists of four number from 0 to 3. The number 0 is given for no lesion, 1 for one to 4 lesions, 2 for 5 to 9 lesions, and 3 for 9 lesions. This scale, however, accounts separately for periventricular corps and deep white matter corps. Deep white matter corps extent is given as 0 for no lesion, 1 for punctuate foci, 2 for beginning confluent foci, and 3 for confluent deep white matter corps while periventricular corps are scored as 1 for caps or pencil-thin lining, 2 for smooth halo, and 3 for irregular periventricular corps extending into deep white matter. Some studies suggest that Fazekas score has the highest inter-observer agreement and correlation with volumetric measurements among rating scales.[6]

Although the FLAIR sequence and the scale of Fazekas are the commonly used methods for the leukoaraiosis volume estimation, it still seems to be a subjective method.

An other way to estimate leukoaraiosis volume is by using computer-based quantitative techniques which were found to be more objective than qualitative and semi-quantitative methods.[7] These methods vary from manual outlining techniques to fully-automatic leukoaraiosis detection.

In our study we combined these two techniques using the advantages of both making a semi-automatic method to enable the leukoaraiosis volume estimation in a more accurate way.

2 Aim

The aim of the study was to test the inter-observer reproducibility of computer-based semi-automatic technique for leukoaraiosis volume estimation on FLAIR sequenced MR scans.

3 Materials and Methods

20 MR brain scans were analyzed with the software *Segmentation Leukoaraiose Adelahyde* from the IADI laboratory. The brain MRI was performed at 1.5T in the axial plane with the slice thickness of 5 mm, as described elsewhere.[8] The segmentation were carried out by two trained observer. Finally, the segmentation were compared and statistically analyzed.

3.1 Population

MRI acquisitions were used from subjects from the Adelahyde study[8]. The ethics committee gave a permission to perform the analysis on them.

Subjects were men and women aged 60 to 85 years with a history of hypertension and subjective memory complaints. They were clinically evaluated, including history recording and a general and neurological examination. Their cognitive status was established by a set of psychometric tests. Exclusion criteria were stroke, heart failure, cancer or systemic diseases, history of nervous system disorders, dementia, depression and history of alcohol or drug abuse.

Out of the population counting 275 patients, we have randomly chosen 20 patients that we used for our analysis.

3.2 Software and Measurement

The software used for the segmentation was a software of the IADI Laboratory called *Segmentation Leukoaraiose Adelahyde* (SLA). This program enables a semi-automatic segmentation of leukoaraiosis.

The analysis were performed in the axial plane. The skull and the surrounding tissue were previously eliminated from the images with a separate software.

During the measurement the SLA software automatically selects the hyper-signal, white pixels. The sensitivity of the automatic selection can be adjusted on each surface at the same time or one by one separately.

However, there are white areas on the MR images, selected automatically by the software, which are not leukoaraiosis plaques. These areas were manually erased. The erased areas were those in the gray matter like in the cerebral cortex and in the basal nuclei.

One advantage of the software is that the contrast can be adjusted, which helps in cases when it is difficult to determine the border of leukoaraiosis areas.

The segmentation were carried out on two consoles paralelly (Figure 3.1). One console was used for segmentation while the other was used for image comparison.



Figure 3.1: The segmentation were carried out on two consoles paralelly.

The two-person group of observers consisted of a resident in radiology and a 3rd year medical student.

Initially 20 images were analyzed but the first 10 image was used only for practicing and to establish the inter-observer consensus and was not included in the statistical analysis. For the inter-observer comparison were used only the second half of the images.

4 Results

The results are shown in Table 1. In each segmentation the higher value is highlighted.

	Leukoaraiosis segmentation values [pixel]	
	<i>Olivier</i>	<i>Katalin</i>
1	414	774
2	3404	3155
3	5708	7545
4	4261	4167
5	3677	5023
6	7250	8900
7	933	672
8	693	1238
9	891	1567
10	1802	2204

Table 1: Leukoaraiosis segmentation values.

There was a statistically significant difference ($p < 0,05$) between the leukoaraiosis segmentation performed by the two observer.

5 Discussion

Segmentation techniques of leukoaraiosis on FLAIR sequences have already been described in several studies.[7] Some of them established that leukoaraiosis segmentation on this sequence is good enough to use it as a standard method.[9] Others showed that even totally automated segmentation techniques have promising results.[10]

However, both the manual outlining technique and the fully-automatic leukoaraiosis detection has disadvantages. These methods are often time consuming, and the reproducibility is not as high as expected. Besides, during a totally automated segmentation, the software is tend to select hyper-signal areas which do not belong to leukoaraiosis regions.[7]

Our software has some advantages compared to softwares already existing. It allows a manually correction of the automatic threshold, and a manual erasement of automatically selected regions, which are considered to be incorrectly selected. Furthermore, in our measurements there was a

possibility to change the contrast which opens an opportunity to do the segmentation even more considerately.

Even though the software has several advantages, the study, investigating its reproducibility, has some limitations. Namely, the little size of the population and the poor experience of observers, which are the major sources of error. The process of setting the threshold by which voxels are estimated to be hyper-intense is susceptible to errors as well resulting from human visual assessing of leukoaraiosis boundaries.

Thus, a further evaluation of the semi-automatic leukoaraiosis segmentation is required with a bigger population, more experienced observers and with several sequences as T2-weighted and density proton sequences. It should be investigated if the negative results are due to the errors in the measurement, the accuracy of the technique, or if the FLAIR sequence is adequate for the leukoaraiosis volume estimation at all.

Diffusion tensor imaging (DTI) is a promising technique as well, which can give information about white matter impairment and micro-architecture.[11] DTI measurements seem to be also correlated to cognitive impairments in elderly subjects.[12] However, it is still not evaluated enough for its utilization in a clinical practice.

6 Conclusion

The study shows a significant lack of reproducibility of the inter-observer leukoaraiosis segmentation on FLAIR sequenced MR scans. It fits in with some other studies, however, it needs to be opposed by studies which are more consequent. DTI seems to be also promising, and a good alternative, but it needs further evaluation for its utilization in a clinical practice.

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