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Technical note

Reference 3 T MRI parameters of the normal human eye

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ABSTRACT

The purpose of this study is to establish magnetic resonance imaging (MRI) standard normative reference quantitative markers for future possible diagnosis in Ophthalmology based on relaxation times (T1 and T2) and retina/choroid complex (RCC) layer thickness values measured *in vivo* in normal human eyes.

This research followed the tenets of the Declaration of Helsinki and was approved by the local Ethical Committee. 15 healthy subjects volunteered to undergo MRI of both eyes. 3 T MRI was performed using a circular surface detector coil with a 15 min acquisition protocol for each eye. The most important normal human eye structures were visualized and characterized geometrico-physicochemically by the 35 MRI standard normative reference markers (20 RCC thicknesses, 8 T1 and 7 T2) calculated. Future possible pathology management could be based on the relative-to-normal differences between the standard normative reference MRI markers calculated in this study and the corresponding MRI markers calculated in the future in disease-suspected eyes.

In conclusion, this research demonstrates that ocular MRI at 3 T, performed without contrast agents, brings useful additional multiparametric quantitative information for future possible automated medical diagnosis, staging and evaluation of ocular disease mechanisms.

1. Introduction

Most of the major health and economic issues with profound socioeconomic consequences worldwide caused by blindness and visual impairment can be avoided, prevented or treated if appropriate programs are to be implemented [34]. Such programs could potentially focus on the implementation of MRI techniques in Ophthalmology [20] due to lower energy deposition in the tissue imaged [19]; [23], no requirement for a transparent light path through the eye during image acquisition [5,30], and deep tissue penetration, allowing for the visualization of both superficial and internal pathophysiology with a wide ranging coverage of physicochemical properties [5].

MRI techniques offer excellent anatomical visualization of various eye structures, in addition to the quantitative information of structural and geometrico-physicochemical properties of the eye in a slice-by-slice manner in a scan time of only a few minutes [11]. To date, this information consists of: detailed eye anatomy, including 3 layers in the RCC region with signal uniformity over the posterior eye segment [32,33], geometrical characterization of the full 3D retinal shape [2], measurements of thicknesses of the layers visualized in the RCC region [32,33], ocular volumes, and sphericity [17,29] along with physicochemical properties of the eye through estimated parameters characterizing: diffusion [16], blood flow ([24,28], and T_1 [12,22,26], and T_2 [12,22] relaxometry.

This study moves ocular MRI one step closer to routine clinical implementation in Ophthalmology and proposes a strategy for ocular MRI at 3 T based on the design of a clinically feasible imaging acquisition protocol, with MRI signal uniformity extended over the entire eye volume and the extraction of statistical quantitative information from as many ocular structures as possible. The main eye structures visualized in this study were: the lens, aqueous humor, iris, cornea, ciliary body, vitreous humor, RCC, sclera, optic nerve, and also 3 layers in the RCC region. The normal human eye was analyzed geometrico-physicochemically through 35 MRI parameters: 20 thicknesses (geometrical) and 15 relaxation times (physicochemical). Physicochemical analysis of ocular physiology was performed through 15 parameters, representing the 8 and 7 mean absolute and relative-to-water T_1 and T_2 measurements in the following normal human eye structures: cornea, lens, ciliary body, aqueous humor, vitreous humor, RCC, sclera (exception: T_2), and optic nerve. Human eye physio-anatomy was assessed geometrically through 20 mean absolute and relative-to-eye axis length thicknesses of the internal (L1), medial (L2), external (L3), and overall (O) layers visualized, measured in five different regions along the length of the RCC: labelled R1 to R5.

2. Materials and methods

This research followed the tenets of the Declaration of Helsinki. All

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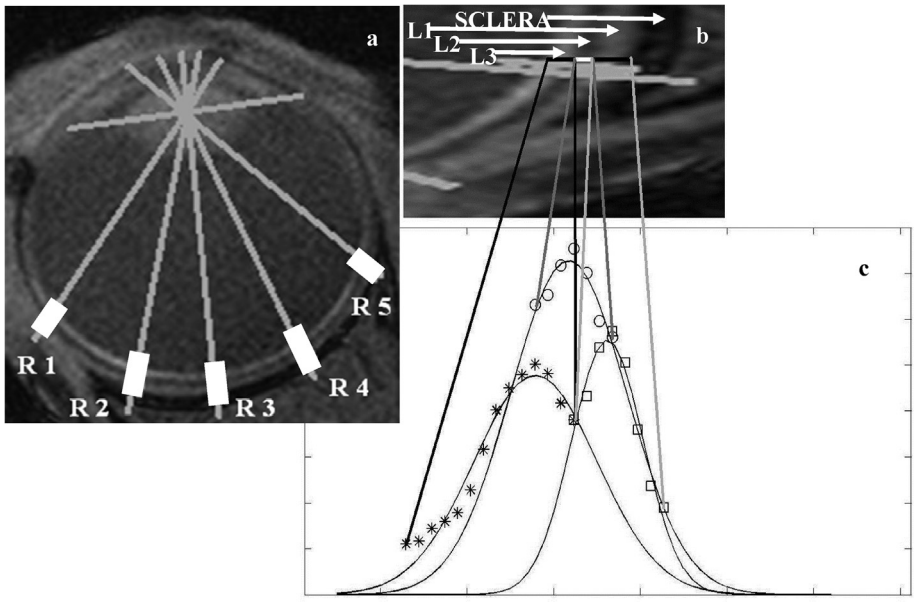

Fig. 1. RCC thickness measurements. A slice from a representative eye image used for the retinal thickness measurements is shown in (a). The eye section was divided into five regions (R1–5) as described in the Methods section. R1 to R5 are defined by the short thick straight white lines superimposed, from the vitreous humor to sclera, on the end of each of the five eye axes in Fig. 1(a). Only two RCC layers were visualized in R1 of the eye presented in Fig. 1(a). A close up view of the retina in region R4 presenting the three RCC layers: (L1–3), and the line profile through the retinal layers in R4, with Gaussian fit to the top exterior lines are presented in (b) and (c). The method for determining the thickness of the central layer is described in the text.

scanning was performed with informed subject consent and approval from the local Ethical Committee. MRI images of both normal eyes of 15 study subjects were acquired using a 3 T MRI system (Achieva, Philips, the Netherlands) and a single loop surface detector coil (diameter 10 cm). Subjects with no personal history of eye disease were included in this study. From the total number of 30 eyes scanned, only 24 and 25 eyes were selected for relaxometry and RCC thickness measurements, respectively, due to magnetic susceptibility and/or motion/blinking artefacts. 8 T_1 and 7 T_2 measurements were performed in the following ocular structures: cornea, aqueous humor, ciliary body, lens, vitreous humor, RCC, sclera (exception: T_2). The 20 RCC markers correspond to the four: O, L1, L2, and L3 RCC thickness measurements in each of the five: R1 to R5 RCC region defined (Fig. 1).

A test tube filled with distilled water was attached to the surface coil and placed above the scanned eye, for use in the standardization of T_1 and T_2 values. The subjects were asked to keep their eyes closed and as relaxed as possible during image acquisition.

The MRI acquisition protocol was developed on appropriate phantoms, and aimed for an optimal compromise between speed of acquisition and image quality. MRI images with spatial resolutions ranging between $0.30 \times 0.30 \times 1.60\,mm^3$ and $0.45 \times 0.45 \times 2.00\,mm^3$ were acquired in 57 to 128 s per eye, using several variants of 3D spoiled gradient recalled echo (SPGR) pulse sequences (Table 1).

T_1 and T_2 maps were obtained using the driven-equilibrium techniques of DESPOT1 and DESPOT2, respectively, which have shown clinical utility in the brain and several other body areas [7]. Relaxometry and RCC layer thickness measurements were performed using: MRIcro (www.cabiatl.com/mricro/mricro), ImageJ (www.imagej.nih.gov/ij), MIPAV (www.mipav.cit.nih.gov), and in-house codes developed in Matlab (The Mathworks, USA).

Pixel-wise T_1 and region of interest (ROI) based T_2 mapping was performed using the DESPOT1 and DESPOT2 methods, respectively [7]. The automatic registration methods in MIPAV were tested on five selected pairs of MRI images used for T_1 mapping. The T_1 values measured using these registration methods were not significantly different than those measured using the non-registered images and, therefore image registration was not performed for T_1 mapping. The two sets of MRI images used for T_2 mapping were first registered using the B-spline automatic registration 2D/3D tool in MIPAV, with *"Normalised Mutual Information"* set as the similarity metric. Stronger susceptibility effects were present on the MRI images used to build the T_2 maps. For this reason, the quality of the T_2 maps was lower than that of the T_1 maps and pixel-wise T_2 mapping was not possible. A segmented approach was, therefore, necessary for the T_2 mapping. ROIs were selected on the non-artefacted regions of the images used for T_2 mapping and the mean values of the signal intensity measured in each of these ROIs was then fitted using the DESPOT2 method to obtain the T_2 value corresponding to each anatomical region. Sclera was not visualized on the images used to obtain the T_2 maps and, therefore, it was not possible to measure the T_2 values in the sclera.

The pixel values in the resultant parameter maps represent the T_1 and T_2 values, in ms, at each pixel location. The mean relaxation time values were then calculated in each ocular structure, based on ROI measurements [22,6]. Both absolute and relative-to-water relaxation time values were determined: the latter represent the percentage difference of the relaxation times in a given ocular structure relative to the corresponding relaxation time of the water.

An image slice corresponding to the largest lens diameter and the best visualization of the eye structures, usually the central eye section, was selected for the thickness measurements. In this image, the eye was divided in distinct regions using two axes: one placed along the long diameter of the eye and the second axis placed perpendicular to the first one and crossing through the centre of the lens, effectively dividing the eye into four regions. In the lower left and right areas, two other axes were drawn at 45° and 22.5° relative to the second axis. These four axes thus divided the RCC into five different regions. This procedure is illustrated in Fig. 1(a). The RCC layer thicknesses were measured in these five regions as follows: for each region, RCC was divided in three layers: internal, medial, and external (Fig. 1b). A signal intensity curve with

Table 1
Details of the MRI protocols. The MRI images in this study were acquired using the 3D SPGR pulse sequence and three imaging protocols: IP1 to IP3. The values of the repetition time (TR), echo time (TE), flip angle (FA), and spatio-temporal resolution for the ocular MRI images acquired for each IP are given below. The RCC and RCC layer thickness measurements were performed on the MRI images acquired using IP1. The T_1 and T_2 maps were generated using IP2 and IP3, respectively.

Imaging protocols: IP	Image parameters			
	TR	TE	FA	Spatiotemporal resolution
	ms	ms	°	mm × mm × mm × s
IP1	13.0	3.3	5,10	0.30 × 0.30 × 1.60 × 128
IP2	5.4	2.8	2,5,15	0.45 × 0.45 × 2.00 × 57
IP3	8.3	4.1	50,60	0.45 × 0.45 × 2.00 × 90