The European Research Journal 2023;9(1):66-72 Original Article

DOI: 10.18621/eurj.1134577 *Radiology*

Evaluation of age-related changes in the vitreous using magnetic resonance imaging

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ABSTRACT

Objectives: Age-related liquefaction of vitreous humor may result in posterior vitreous detachment, retinal tear, and detachment. The purpose of this study is to determine the normative values of age-related changes in the vitreous in the normal population using different MRI sequences.

Methods: A total of 180 eyes of 90 healthy cases were enrolled in this retrospective study. Patients were divided into nine groups according to age, and each group was of equal size with 10 patients(5 male and 5 female). The T1, T2, standardized T1, standardized T2 signals and ADC values determined for each vitreous humor of each eye. MRI parameters of the vitreous were compared within and between age groups.

Results: No difference was detected within the decadic age groups for mean T1W for the right and left (p = 0.912 and p = 0.903, respectively), T2W for the right and left (p = 0.966 and p = 0.983, respectively), standardized T2W for the right and left (p = 0.915 and p = 0.899, respectively), and ADC for right and left values (p = 0.622 and p = 0.524, respectively). A significant difference was found between decadic age groups in terms of the standardized T1W values for right and left ($p < 0.001$ and $p < 0.001$, respectively). Standardized T1W values of vitreous fluid show a moderate degree of correlation with age for the right (r = 0.514, $p < 0.001$) and left eyes (r = 0.534, $p < 0.001$).

Conclusions: This study provides comprehensive normative data on the different MRI signal properties of the human vitreous and its change with age. Using MRI, especially with standardized T1 measurements, age-related changes in the vitreous humor can be revealed non-invasively.

Keywords: Aging, eye, diffusion-weighted imaging, MRI, vitreous humor

The vitreous makes up 80% of the globe and is the largest structure of the eye. Essentially, it consists of water, collagen, and hyaluronic acid groups and it is in a homogeneous gelous form during childhood. Deterioration of this gel structure and resulting inhomogeneity is termed liquefaction and this condition increases with increasing age. Albeit the mechanism of liquefaction is not known precisely, increased amounts of collagen and increased collagen bond ratio are considered among potential factors [1, 2].

Age-related liquefaction of vitreous humor is clinically important as it may result in posterior vitreous detachment, retinal tear and detachment. Therefore, assessment of the vitreous can provide early diagnosis

Received: ***June 23, 2022;*** *Accepted:* ***August 20, 2022;*** *Published Online:* ***September 19, 2022***

How to cite this article: *Kuzan BN, Kuzan TY, Buğdaycı O. Evaluation of age-related changes in the vitreous using magnetic resonance imaging. Eur Res J 2023;9(1):66-72. DOI: 10.18621/eurj.1134577*

e-ISSN: 2149-3189

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and treatment of pathologies in the vitreous and adjacent structures [3]. The vitreous can be evaluated using invasive techniques such as vitrectomy or vitreous fluid sampling, but aside from being invasive, this involves several risks such as hemorrhage, retinal rupture and detachment [4]. Magnetic Resonance Imaging (MRI), allows protein and water content to be evaluated noninvasively. Increased protein and decreased water percentage, which occurs especially with aging, can be shown as an increase in signal on T1 (spin-lattice interaction) weighted sequences on MRI [5].

The objective of this study is to reveal the normative values of age-related changes in the vitreous in the normal population on different MRI sequences and to explore its correlation with age.

METHODS

Patient Selection

This retrospective study was approved by the local Ethics Committee (Decision no: 09.2020.1072). Patients who underwent brain MRI between January 1, 2020, and November 1, 2020 and demonstrated no abnormality on imaging formed our study population. Patients with any history of neurological or ophthalmological disease that might impact cerebrospinal fluid (CSF) or vitreous humor and those with a history of malignancy and chronic disease were excluded from the study. MRI examinations which contained artifacts or were non-diagnostic were also excluded from the study. From this population, 90 patients were randomly selected according to their age. Patients were divided into 9 age groups based on the decade of their age, each consisting of 10 individuals (groups 1-9, respectively). Equal gender distribution was achieved, with 5 females and 5 males in each group.

Equipment and MRI Examination

All images were obtained on 1.5 T MRI devices (Ingenia; Philips Healthcare, Cleveland, Ohio). Routine brain sequences were acquired using 8 and 16-channel head coils. In the examinations, T1-weighted (T1W), T2-weighted (T2W), Diffusion-weighted images (DWI) and Apparent Diffusion Coefficient (ADC) maps were obtained (SE T1 axial, TR/TE 324/9, FA: 90, slice thickness 5.5 mm, gap 1.6 mm; TSE T2 axial, TR/TE 3790/89, slice thickness 5.5 mm, gap 1.6 mm). The b0 and b1000 values were used for diffusion imaging (SE FS DWI axial, TR/TE 3230/85, FA: 90, slice thickness 5 mm, gap 1 mm).

Image Interpretation

The brain MRI images were transmitted to the workstation and picture archiving and communication system (Infinitt PACS; Infinitt Healthcare, Seoul, South Korea). Images were evaluated by a radiologist with 5 years of experience, blinded to the patient information. The axial T1W and T2W sequences and ADC maps where the globe was seen at its largest diameter were chosen for evaluation. Measurements were performed by drawing the largest oval or round "region of interest" (ROI) possible in the vitreous, without extending beyond the globe. Three measurements were taken for each image sequence and for each orbit and the mean signal value was recorded. The minimum, maximum, median values and standard deviations of each measurement were recorded. In order to normalize differences between individuals due to local magnetic inhomogeneities, standardized T1W and T2W values were computed separately for the right and left by proportioning the vitreous T1W,

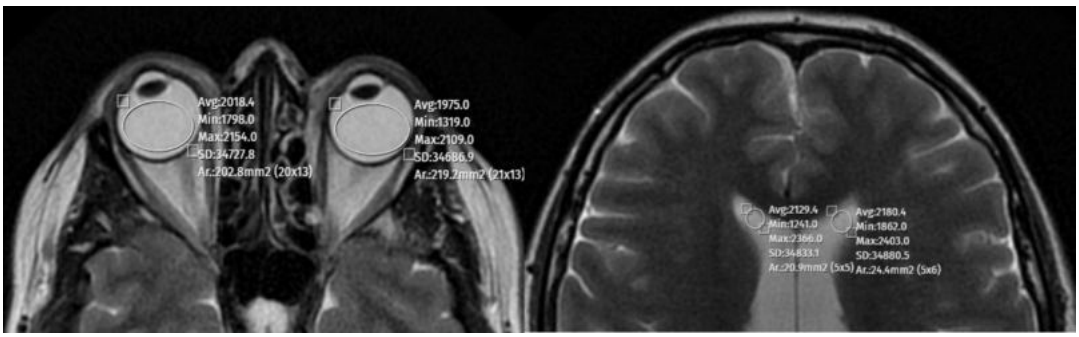


Fig. 1. An example of measurement of T2 values of vitreous and cerebrospinal fluid in axial sections.

T2W signal values to the values of the CSF at the level of the ipsilateral lateral ventricular frontal horn (Fig. 1).

Statistical Analysis

Whether the data conformed to the normal distribution was analyzed via the Kolmogorov–Smirnov test. Data not showing normal distribution were analyzed with the Pearson correlation test, and r coefficients and p values were calculated. The regression coefficient was calculated by conducting regression analysis between age and vitreous values, and the regression equation was established. Vitreous humor values between decades were compared with the ANOVA test and post hoc analysis was made. The results were considered statistically significant at $p < 0.05$. SPSS 17.0 (IBM Inc., Armonk, NY, USA) was used for the statistical analysis.

RESULTS

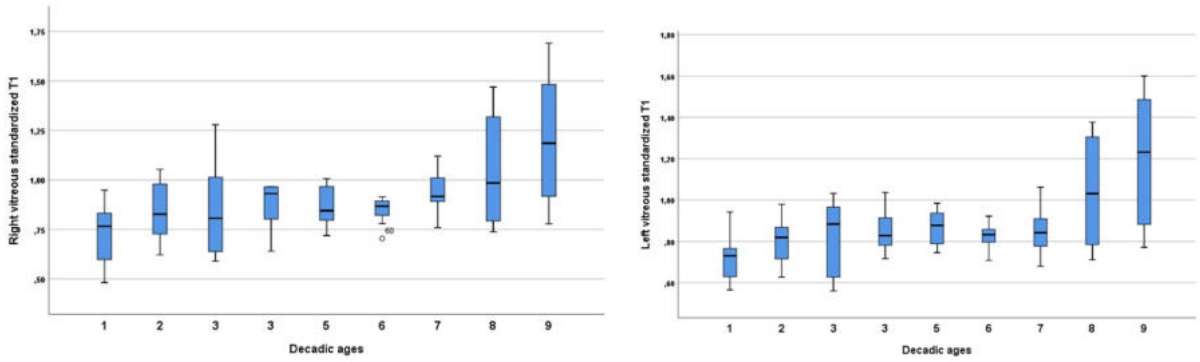
A total of 90 patients, 45 male, and 45 female, aged between 0 months and 87 years were included in the study. Each of the 9 decadic age groups consisted of 5 males and 5 females. The mean age of all patients was 43.6 ± 25.5 years.

The mean T1W value of the vitreous fluid was measured as 149.9 ± 55.1 in the right eye and 146.9 ± 52.1 in the left eye, and no difference was detected between the decadic age groups in terms of the mean T1W values for the right and left ($p = 0.912$ and $p = 0.903$, respectively). Likewise, the mean T2W value of the vitreous fluid was measured as 839.9 ± 349.1 in

Tables 1. Standardized T1, standardized T2 and ADC values of the cases according to decades for right and left eyes

	Right vitreous standardized T1				Right vitreous standardized T2				Right vitreous ADC			
Decadic Age Groups (year)	**Mean**	**SD.**	**Min.**	**Max.**	**Mean**	**SD.**	**Min.**	**Max.**	**Mean**	**SD.**	**Min.**	**Max.**
1 (0-10)	.736	.150	.48	.95	.844	.126	.58	.98	3291.10	294.89	2741.46	3695.15
2 (11-20)	.845	.151	.62	1.05	.785	.194	.52	.99	3443.38	175.82	3159.45	3716.12
3 (21-30)	.846	.223	.59	1.28	.824	.152	.57	.96	3395.18	318.27	3037.15	3905.89
4 (31-40)	.867	.126	.64	.97	.815	.167	.61	1.11	3310.01	237.68	2972.73	3620.99
5 (41-50)	.865	.098	.72	1.01	.878	.154	.60	1.01	3280.94	222.95	3054.48	3594.87
6 (51-60)	.849	.065	.70	.92	.832	.144	.64	1.01	3222.87	286.51	2882.11	3675.43
7 (61-70)	.942	.107	.76	1.12	.848	.139	.65	.97	3325.18	300.01	2885.52	3734.04
8 (71-80)	1.059	.284	.74	1.47	.835	.186	.60	1.10	3218.05	222.76	2966.31	3521.52
9 (81-90)	1.208	.340	.78	1.69	.914	.318	.60	1.70	3254.59	327.67	2834.66	3815.86
	Left vitreous standardized T1				**Left vitreous standardized T2**				**Left vitreous ADC**			
Decadic Age Groups (year)	**Mean**	**SD.**	**Min.**	**Max.**	**Mean**	**SD.**	**Min.**	**Max.**	**Mean**	**SD.**	**Min.**	**Max.**
1 (0-10)	.726	.120	.57	.94	.820	.108	.64	.96	3301.39	292.52	2873.09	3642.84
2 (11-20)	.807	.118	.63	.98	.805	.172	.56	1.04	3484.87	183.73	3261.11	3793.10
3 (21-30)	.821	.179	.56	1.03	.834	.125	.62	.99	3390.15	309.98	2948.89	3825.00
4 (31-40)	.849	.103	.72	1.04	.782	.121	.60	.95	3316.97	241.84	2957.06	3650.26
5 (41-50)	.866	.085	.75	.98	.860	.135	.60	1.02	3286.67	262.00	2984.86	3630.66
6 (51-60)	.825	.064	.71	.92	.833	.110	.67	.96	3232.75	305.25	2855.52	3716.48
7 (61-70)	.849	.109	.68	1.06	.839	.140	.61	.98	3341.04	300.27	2907.75	3738.90
8 (71-80)	1.047	.268	.71	1.38	.790	.162	.60	1.01	3210.80	232.12	2957.10	3667.89
9 (81-90)	1.186	.322	.77	1.60	.888	.289	.62	1.64	3331.24	306.06	2850.79	3873.54

SD = standard deviation, Min. = minimum, Max. = maximum



a b

Fig. 2. Box-line plot of standardized T1 values of vitreous humor according to decades for right (a) and left (b) eyes.

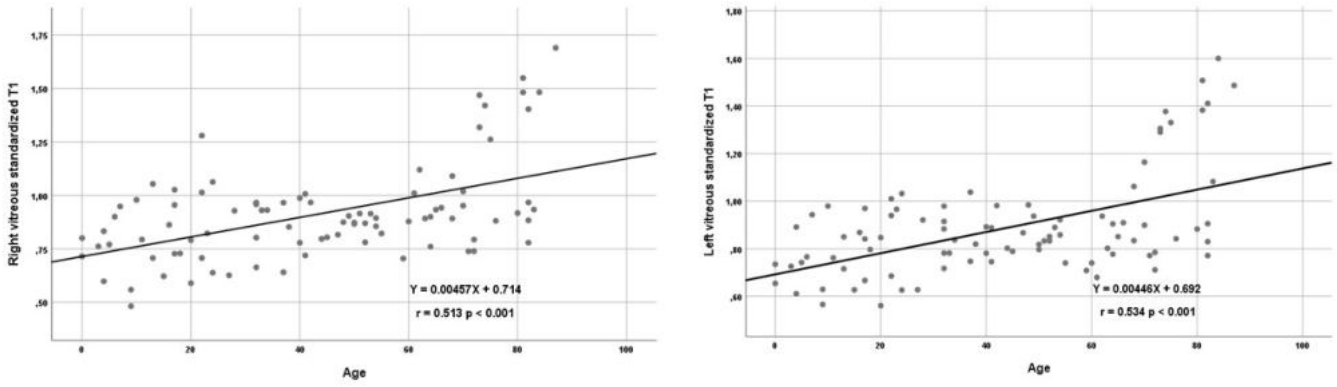
the right eye and 836.7 ± 358.7 in the left eye, and no difference was determined between the decadic age groups regarding the mean T2W values for the right and left ($p = 0.966$ and $p = 0.983$, respectively).

Standardized T1W values of vitreous fluid obtained by dividing T1W values of vitreous fluid by CSF T1W values are presented in Table 1 for all patients according to decadic age groups. Standardized mean T1W values of vitreous fluid were measured as 0.913 ± 0.226 in the right eye and 0.887 ± 0.213 in the left eye, and a significant difference was determined between decadic age groups in terms of the standardized T1W values for right and left ($p < 0.001$ and $p < 0.001$, respectively). Post hoc analysis of mean standardized T1W values revealed that group 9 (81-90 years) values were significantly different for both eyes from all age groups except group 8 (71-80 years) ($p < 0.05$) (Fig. 2). The mean standardized T1W values observed in group 8 (71-80 years) were found to be different from group 1 for both eyes ($p < 0.05$).

The standardized mean T2W values of the vitreous were measured as 0.842 ± 0.179 in the right eye and 0.828 ± 0.157 in the left eye, and no difference was determined between the decadic age groups regarding

Table 2. Correlation of different magnetic resonance imaging (MRI) variables with ages for rigth and left eyes

Variables		Age (Right Vitreous)	Age (Left Vitreous)
Vitreous T1	r	.070	.075
	p value	.511	.481
Cerebrospinal fluid T1	r	-.165	-.167
	p value	.120	.115
Standardized T1	r	.515	.534
	p value	**< 0.001**	**< 0.001**
Vitreous T2	r	-.042	-.060
	p value	.694	.576
Cerebrospinal fluid T2	r	-.070	-.067
	p value	.514	.530
Standardized T2	r	.130	.091
	p value	.220	.393
Vitreous ADC	r	-.171	-.140
	p value	.107	.188



a **b**

Fig. 3. Pearson linear regression plot between age and vitreous humor standardized T1 values for right (a) and left (b) eyes.

the standardized T2W values for the right and left (p = 0.915 and p = 0.899, respectively).

Mean ADC values of vitreous were found to be 3304.6 ± 266.9 mm^2/s for the right eye, and 3321.7 ± 272.2 mm^2/s for the left eye, and no significant difference was found between decadic age groups in terms of ADC value for right and left (p = 0.622 and p = 0.524, respectively).

Standardized T1W values of vitreous fluid demonstrated moderate correlation with age for both the right (r = 0.514, $p < 0.01$) and left eyes (r = 0.534, $p < 0.01$). Other measurements did not correlate with age (Table 2). Linear regression models, showed that every one year increase in age corresponded to an increase of 0.0045 units in standardized T1 value of vitreous for the right and left eyes (CI: 0.632 to 0.796; $p < 0.001$ and CI: 0.617 to 0.768; $p < 0.001$, respectively) (Fig. 3).

DISCUSSION

In this study, normative values of age-related changes in the vitreous in the normal population were calculated for different MRI sequences, and standardized T1W values were found to be correlated with age.

This age dependent change in the vitreous can be explained by ongoing liquefaction with aging [6]. The first theory regarding the gelous structure of the vitreous, was put forward by Duke-Elder and is widely accepted today. According to the theory, 'the structure of the vitreous consists of loose and sensitive filaments surrounded by liquid' [7]. Subsequently, in the 17th-18th centuries, different morphological and histological characteristics of the vitreous were described by Alveolar theory, Lamellar theory, Radial sector theory, and Fibrilar theories [8]. Accordingly, it was suggested that the vitreous was homogeneous in volunteers under 30 years of age, while macroscopic fibers were located centrally in the middle-aged group. With aging, thickening of the fibers and development of tortuosity has been observed, and a decrease in vitreous volume and collapse have been described with the surrounding of the fibers by the vitreous [9]. Balazs *et al*. [10] reported that the fibrils degenerated and liquid lacunae formed around them in the 80-90 age group, and that half of the vitreous was liquid. Likewise, in our study, standardized T1W values increasing with growing age also support this reorganization in the fibrillar structure.

Collagen is a key component in the fibrillar vitreous structure and with aging, the collagen component on the fibril surface decreases. Collagen fibrils, which break up and form small fragments due to age-related liquefaction, form aggregates to preserve the non-liquefacted gelatinous vitreous structure [11]. Hyaluronic acid is another key ingredient in the vitreous and contributes to its viscosity. The decrease of hyaluronic acid and proteoglycans with aging leads to liquefaction, which could be associated with an increase in standardized T1 values, as in our study [12].

In addition to conventional and modern histological examinations, microscopic and ophthalmoscopic examinations are also used in the evaluation of the vitreous [13]. MRI, however, allows non-invasive examination of the entire the globe structure, the vitreous,

as well as the extra-orbital area. Currently, 1.5 T and 3 T devices can be used for orbital imaging, and image resolution improves with 3 T MRI due to its stronger magnetic field. However, as the magnet power increases, the sensitivity to magnetic inhomogeneity also increases and it becomes more susceptible to possible artifacts. Orbit is a region where MRI artifacts are frequently seen because of the air-filled paranasal sinuses and bone structure around it. As a consequence of this, distortion due to magnetic susceptibility artifact is more common in images obtained on 3T devices. Although this situation sometimes reduces the detectability of lesions, artifacts that may occur can be prevented with the use of appropriate coils and extraction techniques [14]. Lesions can be identified in sequences such as T1W, T2W, and DWI, and pathological contrast enhancement can be demonstrated in the lesion after intravenous contrast agent (IVCM) administration [15]. Since it does not require ionizing radiation, it can be used in different age groups, and signal changes due to aging can be evaluated using MRI. Revealing these changes with MRI could allow early diagnosis and treatment.

In MR examinations, the vitreous signal was is seen as hyperintense in T2W examinations due to its high (98%) water content, while it is hypointense in T1W examinations compared to the extraocular muscles [15]. The studies in the literature on age-related changes in the vitreous are limited. In the study conducted by Kupeli *et al*. [16] on aging and changes in the vitreous, a positive correlation was found between the increasing age and ADC values after the third decade, whereas no significant difference was found between ADC values in the first three decades, showed a significant difference. In the study by Meral *et al*. [17], a significant difference was reported between pediatric and adult groups regarding ADC values.However, there was no regular increase in ADC values with age. Similarly, no significant correlation was found between ADC values and decadic age groups in our study. This situation can be explained by vitreous heterogeneity and disorganized diffusion environment as a result of liquefaction occurring with aging.

In the literature, there is no detailed information on T1W and T2W MRI signal changes that occur in the vitreous with aging. In our study, an increasing trend was observed in the standardized T1W values of decadic age groups, and a moderate positive correlation was determined between standardized T1W values and age. This can be explained by the structural change of protein groups in the vitreous with aging and the relative increase due to the decreasing amount of free water. On the other hand, no significant difference was found between decadic age groups in terms of T2W signals. The lacunae that form due to liquefaction over time might not sufficiently alter the already high T2W signal of the healthy vitreous.

Limitations

The limitations of the study include the relatively small number of patients included in the study and the inability to calculate interobserver compliance due to the evaluation of imaging by a single radiologist. Furthermore, the images were obtained from a 1.5T scanner and results might vary or additional correlations might be found on higher field strength scanners.

CONCLUSION

In conclusion, our study provides comprehensive normative data on the different MRI signal properties of the human vitreous and its change with age. Aging-related changes in the vitreous can be non-invasively assessed by MRI, particularly with standardized T1W values. MRI could provide an opportunity for earlier diagnosis and treatment of the pathological conditions of the vitreous. The information obtained from our study could serve as a basis for further studies aimed specifically at identifying vitreous MRI signal properties.

Authors' Contribution

Study Conception: BNK, OB; Study Design: BNK, TYK; Supervision: OB, FE; Funding: N/A; Materials: N/A; Data Collection and/or Processing: BNK; Statistical Analysis and/or Data Interpretation: TYK; Literature Review: BNK, TYK; Manuscript Preparation: BNK, TYK and Critical Review: OB.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any

grant during conduction or writing of this study.

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