Diffusion Changes in the Vitreous Humor of the Eye during Aging

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BACKGROUND AND PURPOSE: The inability to image the vitreous humor of the eye adequately hinders a complete understanding of its normal structure and the changes occurring in aging and disease. The purpose of the present study was to reveal normative data and age-related changes of the vitreous humor by using DWI.

MATERIALS AND METHODS: A total of 160 patients were enrolled in the present study. Patients were divided into 8 groups according to decade of age, and each group was of equal size with 20 patients. The ADCs were determined for each vitreous humor. Each determination was obtained by using average regions of interest of 50 ± 2 mm². ADC values were then plotted against age.

RESULTS: The ADC values obtained from group 0 (0–10 years of age) were statistically different from those of all other groups (P < .05). Group 1 (11–20 years of age) was statistically different from groups 3, 5, 6, and 7 (P < .05). A trend toward increased ADC values with increasing age was not statistically significant.

CONCLUSIONS: Besides the statistically significant difference between pediatric and adult patients, a statistically insignificant trend of increased ADC values among aging adults has been demonstrated. These normative data contribute to our understanding of how DWI can aid in the diagnosis of age-related changes in eye health and function.

Abbreviations: ADC = apparent diffusion coefficient; DWI = diffusion-weighted imaging; OCT = optical coherence tomography; SLO = scanning laser ophthalmoscopy

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Mean ADC values for each group*

<table>
<thead>
<tr>
<th>Decadic Age Groups (yr)</th>
<th>Mean ADC Value ((\times 10^{-3} \text{ mm}^2/\text{s})) (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 0 (0–10)</td>
<td>3.02 (\pm) 0.07 (2.88–3.16)</td>
</tr>
<tr>
<td>Group 1 (11–20)</td>
<td>3.28 (\pm) 0.07 (3.15–3.41)</td>
</tr>
<tr>
<td>Group 2 (21–30)</td>
<td>3.39 (\pm) 0.07 (3.26–3.52)</td>
</tr>
<tr>
<td>Group 3 (31–40)</td>
<td>3.59 (\pm) 0.07 (3.46–3.72)</td>
</tr>
<tr>
<td>Group 4 (41–50)</td>
<td>3.31 (\pm) 0.08 (3.15–3.48)</td>
</tr>
<tr>
<td>Group 5 (51–60)</td>
<td>3.62 (\pm) 0.07 (3.48–3.76)</td>
</tr>
<tr>
<td>Group 6 (61–70)</td>
<td>3.56 (\pm) 0.07 (3.43–3.69)</td>
</tr>
<tr>
<td>Group 7 (71+)</td>
<td>3.57 (\pm) 0.07 (3.44–3.70)</td>
</tr>
</tbody>
</table>

*The ADC values obtained from group 0 were statistically different from those in the other groups, whereas group 1 was statistically different from groups 3, 5, 6, and 7 \((P < .05)\). An observable trend showing increasing ADC values with increased aging is not statistically significant.

The data evaluators were blinded to the age of the patient when calculating ADC values for each vitreous humor. The mean values of the areas corresponding to a region of interest of 50 \(\pm\) 2 mm² were calculated. Interobserver and intraobserver variability of ADC values were tested by using Cronbach \(\alpha\). ADC values obtained from the vitreous humor of the right and left eyes in each patient were analyzed by using paired \(t\) tests. Mean ADC values grouped in decadic ages of life were then compared by using multivariate analysis of variance. The significance level for assessing meaningful differences was \(P < .05\).

Results

Our study population consisted of 160 patients, 74 males and 86 females, ranging in age from 2 months to 84 years. The mean age of all patients was 40 \(\pm\) 18 years.

The internal control group consisted of 20 patients, 8 males and 12 females, ranging in age from 16 to 63 years with a mean age of 36.7 \(\pm\) 17 years. The mean ADC value obtained from CSF was 3.48 \(\pm\) 0.05 \(\times\) 10⁻³ mm²/s (range, 2.35–4.31 \(\times\) 10⁻³ mm²/s) and, for the vitreous, 3.35 \(\pm\) 0.02 \(\times\) 10⁻³ mm²/s (range 2.88–3.77 \(\times\) 10⁻³ mm²/s). While the mean ADC value of the vitreous was lower than that of the CSF, the difference was not statistically significant \((P > .05)\).

The Table presents the mean (plus the measure of variation) of the ADC values obtained for all study patients organized into decadic age groups. Post hoc analysis of the mean ADC values revealed that those of group 0 (0–10 years) were statistically different from the mean ADC values of all other age groups \((P < .05)\) (Fig 1A, B). The mean ADC value observed in age group 1 (11–20 years) was found to be different from those of groups 3, 5, 6, and 7 as well \((P < .05)\). While the mean ADC values of groups 2 and 4 were seen to be higher than that in group 1, this difference was not statistically significant.

Differences in the ADC values between the right and left eyes of each patient were assessed and found not to be significantly different \((P > .05)\). Moreover, there were no statistically significant differences in the inter- or intraobserver ADC value determination \((\alpha\) : 0.82 and 0.86, respectively). While a trend could be observed in that ADC values increased with healthy patient age, the statistical significance of this correlation could not be established.

Discussion

The vitreous humor of the eye is composed of a transparent gel consisting almost entirely of the constituents that describe tissue extracellular matrix. It is composed largely of water with small amounts of essential structural macromolecules. The gel state of the vitreous humor is maintained by a low-attenuation network of long thin collagen fibrils.

The vitreous gel, which is quite compositionally homogeneous with no relative liquefaction in infancy, undergoes noticeable age-related changes with the progress of years. Morpherologically, 2 distinct structural alterations can be observed. On the 1 hand, there is a progressive increase in the volume of liquefied spaces (synchysis), and on the other, there is an increase in optically attenuated areas (syneresis). Collagen fibrils are an essential component of the vitreous gel structure, and with time, they break down into smaller fragments that are involved in the mechanism of the age-related liquefaction of the vitreous humor. With aging, these collagen fibrils progressively aggregate due to a loss of collagen components on the fibril surface necessary for maintaining a nonliquefied gelatinous state. In particular, hyaluronic acid is a major component of the vitreous gel, which contributes to gel viscosity, and both this substance and proteoglycans decrease in the

![Fig 1. A, ADC values obtained from the vitreous of a 4-year-old girl (W 1524/L 762). B, ADC values obtained from the vitreous of a 54-year-old man (W 1528, L 764).](www.ajnr.org)
content of the gel and may explain age-related vitreous liquefaction. 2,4

Diffusion is a physical property, which describes the microscopic random movement of (water) molecules driven by their internal thermal energy. Relative free or unimpeded diffusion is encountered in tissues with low cellularity or tissues with disrupted cell membranes, as in cysts and necrotic tissues.15,16

Diffusion can be quantitatively evaluated by using ADC, expressed in square millimeters per second. The ADC reflects disrupted cell membranes, as in cysts and necrotic tissues.15,16

DWI has been a complementary technique useful in the differential diagnosis of orbital pathologies such as orbital tortuosity, intracellular restrictions, membrane permeability, active processes across membranes, relaxation rates, or anisotropic morphology.17 A low ADC value implies a limited or restricted diffusion, and this is observed in tissues that are highly cellular. A high ADC value is more likely seen in structures in which tissue fluid has relatively free diffusion, in those with low cellularity, or in those that are cystic.15,16

Intravoxel incoherent motion (IVIM) is a method of diffusion that characterizes changes in the vitreous humor occurring by the end of the second decade of life, the normative data of the vitreous humor may play a complementary role not only for the differential diagnosis of ocular pathologies but also in contributing information to a large data base looking at how aging affects the vitreous humor.

**Acknowledgments**

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**References**


17. Meier C, Dreher W, Leibfritz D. Diffusion in compartmental systems. I. A Furthermore, the study has revealed a certain degree of vitreal liquefaction that occurs by the end of the second decade, DWI is unable to further characterize changes in the vitreous. This seems to be a limitation of the study. However, this normative data does have potential use for assessing patients with eye disease.

**Conclusions**

A better understanding of the normal physiology and structure of the vitreous humor of the eye and how changes in structure and function occur during aging and disease is necessary to develop more effective therapies and preventative care. Our use of DWI gave results that indicated a trend, though not statistically significant, showing increases in ADC values with advancing age, and we did find statistically significant difference between decadal age groups, namely between pediatric and adult patients. While DWI is unable to further characterize changes in the vitreous humor occurring by the end of the second decade of life, the normative data of the vitreous humor may play a complementary role not only for the differential diagnosis of ocular pathologies but also in contributing information to a large data base looking at how aging affects the vitreous humor.


