

UDC: 616-006.487

Y. V. FILIPPENKO^{1,2}, ZH. ZH. ZHOLDYBAY^{1,2}
¹Kazakh Institute of Oncology and Radiology, Almaty, the Republic of Kazakhstan

²JC National Medical University, Almaty, the Republic of Kazakhstan

The capacity of MRI in diagnosing retinoblastoma (literature review)

Introduction. *Retinoblastoma is the most common malignant tumor of the retina and accounts for about 2.5% of all malignant neoplasms in children. Since computed tomography (CT) is associated with an increased long-term risk of malignancy in young patients, magnetic-resonance imaging (MRI) is the major modern method of retinoblastoma diagnostics.*

Purpose of this study is to review the capacity of MRI in diagnosing retinoblastoma.

Results. *MRI is distinguished by an absence of harmful radiation and a high resolution for soft tissue. MRI can improve diagnostics of the stage of tumor process by providing a detailed information for the evaluation of intraocular tumor spread (into the choroid, sclera and/or prelaminar part of the optic nerve) and extraocular (post-laminar or orbital invasion) or intracranial invasion (pineoblastoma, or metastases).*

Conclusion. *MRI is an essential method of retinoblastoma diagnostics and staging of the tumor process. It increases the chances of preserving the eye and vision in children.*

Keywords: *magnetic-resonance imaging (MRI), retinoblastoma.*

Introduction. Retinoblastoma is the most common intraocular malignant neoplasm in children [1]. The main strategy in treating retinoblastoma is to save the child's life through early tumor detection and the prevention of metastasis [2]. The authors report that the diagnostic sensitivity of magnetic resonance imaging (MRI) in detection of high risk signs, including postlaminar optic nerve, choroidal and scleral invasion, is 59%, 74% and 88%, respectively [3]. Therefore, the topic of our review is to reveal the MRI capacity in diagnosing retinoblastoma.

Material and methods. The literature search was done in PubMed database for 2000-2018 by the keywords "Retinoblastoma, MRI". This literature review includes 33 literature sources meeting the relevant selection criteria: original scientific articles containing the analysis of MRI results in retinoblastoma.

Literature review. Retinoblastoma is the most common intraocular malignant neoplasm in children [4-8]. Its incidence has grown twice in the recent decades. In 1980s, this tumor was diagnosed in 1/34,000 newborns; today, it reaches 1/15,000–20,000 newborns [9]. Worldwide, the survival rate after retinoblastoma varies markedly: from about 30% in Africa up to 60% in Asia, 80% in Latin America, and 95%–97% in Europe and North America [10].

80% of retinoblastoma cases are diagnosed before the age of 3 years, 95% of cases – before the age of 5 years. In spite of some reports about retinoblastoma cases in adults, the onset of the disease at the age after 6 years is quite rare [11-13]. The process is bilateral in about 30% of cases. The lesions can be synchronous, metachronous, unifocal, or multifocal. No racial or sexual predisposition has been determined for this type of cancer [14].

Retinoblastoma is usually diagnosed by indirect ophthalmoscopy. Still, additional imaging techniques are indispensable for its diagnostics [15]. Currently, MRI is the most common method of retinoblastoma diagnostics since computed tomography (CT) is associated with an increased long-term risk of malignancy in young patients [11-13].

The main advantages of MRI are: no harmful radiation and high resolution for soft tissues [16-18]. In the cases of

the unclear optical medium and when a growing tumor blocks the view of the optical disk, only MRI allows detecting infiltration before the optic nerve laminar part [19-21]. MRI can better determine tumor stage by providing detailed information for the assessment of intraocular tumor invasion (into choroid, sclera and/or optic nerve prelaminar part), as well as its extraocular (postlaminar or orbital invasion) or intracranial invasion (pineoblastoma or mts) [16-18].

MRI of at least 1.5 T is required for efficient visualization of initial signs of tumor infiltration. This can be achieved by using surface coils and high-resolution protocols. 3T MRI can provide the same resolution without surface coils [22].

On T2-weighted MRI image, retinoblastoma usually delivers a lower signal compared to the vitreous. On T2-weighted gradient-echo and non-3D FSE T2-weighted images, partially calcined areas can be represented as hypointense foci inside the tumor. On T1-weighted image, retinoblastoma delivers a poorly hyperintense signal compared to the vitreous. The vitreous can be unnaturally bright on T1-weighted images due to the increased content of globulin and the reduced albumin/globulin ratio at malignant tumors. On diffusivity maps, the tumor has a lower diffusion coefficient vs. the vitreous. Retinoblastoma is a round shape tumor which is normally poorly differentiated, tightly packed and has a high atomic-cytoplasmic structure. The latter could explain its low diffusion coefficient [15, 23-25].

Amplification of the anterior ocular segment is a distinctive feature of a progressive retinoblastoma. It correlates with the tumor volume and the invasion into the optic nerve. The amplification can be moderate (36%) or strong (33%). It reflects the angiogenesis, hyperemia and inflammation of the iris [26-28]. The MR-measured values of the axial length, equatorial diameter, and volume of the eyes are significantly less in retinoblastoma eyes vs. healthy eyes. Furthermore, size of the eye in patients with retinoblastoma is inversely proportional to the tumor volume [29].

Retinoblastoma shall be differentiated from other intraocular formations accompanied with leukocoria. Retinoblastoma is the most common cause of leukocoria

(56-72% cases). Other causes include: the persistent hyperplastic primary vitreous (19-28%), the coloboma (11.5%), the sclerosing endophthalmitis (6.5-16%), the Coats' disease (4-16%), the retinal astrocytoma (3%), the medulloepithelioma, the retinal dysplasia in the form of Walker-Warburg syndrome and Noir's syndrome, as well as the retrolental fibroplasia of preterm newborns [14, 30].

Special software providing diffusion-weighted images (DWI) is used to improve the quality of imaging of the tumor process in addition to the standard protocol. DWIs are based on the diffusion of water molecules in tissues; the water diffusion in tumor tissues is associated with the tumor cellularity [16-18].

The DWI-associated water diffusion map can grow after successful treatment reflecting the decline of cell density and the water barrier. Therefore, the DWI and water diffusion values can be used to differentiate the tumor zones with high cell density from cell-free areas and evaluate the response to treatment in the form of cell changes within the tumor [31].

Early diagnostics provides good chances for preserving the eye and the remaining vision and possible survival in more than 95% of cases [32].

Conclusion. Thus, MRI is an essential method for retinoblastoma diagnostics and definition of the tumor staging as it increases the chances of preserving the eye and vision in children.

References:

- Houston S.K., Murray T.G., Wolfe S.Q., Fernandes C.E. Current update on retinoblastoma // *Int Ophthalmol Clin.* – 2011. – Vol. 51. – P. 77–91;
- Soliman S.E., Racher H., Zhang C. et al. Genetics and molecular diagnostics in retinoblastoma – an update // *Asia Pac J Ophthalmol (Phila).* – 2017. – Vol. 6. – P. 197–207;
- de Jong M.C., de Graaf P., Noij D.P. et al. Diagnostic performance of magnetic resonance imaging and computed tomography for advanced retinoblastoma: a systematic review and meta-analysis // *Ophthalmology.* – 2014. – Vol. 121. – P. 1109–1118;
- Rodriguez-Galindo C., Orbach D.B., Vander Veen D. Retinoblastoma // *Pediatr Clin North Am.* – 2015. – Vol. 62. – P. 201–223;
- Abramson D.H. Retinoblastoma: saving life with vision // *Annu Rev Med.* – 2014. – Vol. 65. – P. 171–184;
- Dimaras H., Kimani K., Dimba E.A., Gronsdahl P., White A., Chan H.S., Gallie B.L. Retinoblastoma // *Lancet.* – 2012. – Vol. 379. – P. 1436–1446;
- Rauschecker A.M., Patel C.V., Yeom K.W., Eisenhut C.A., Gawande R.S., O'Brien J.M., Ebrahimi K.B., Daldrup-Link H.E. High-resolution MR imaging of the orbit in patients with retinoblastoma // *Radiographics.* – 2012. – Vol. 32. – P. 1307–1326;
- Asnaghi L., Tripathy A., Yang Q., Kaur H., Hanaford A., Yu W., Eberhart C.G. Targeting Notch signaling as a novel therapy for retinoblastoma // *Oncotarget.* – 2016. – Vol. 7. – P. 70028–70044;
- Federal'nye klinicheskie rekomendatsii «Diagnostika, monitoring i lechenie detey s retinoblastomoy» (natsional'nyy protokol) [Federal Clinical Guidelines "Diagnostics, monitoring and treatment of children with retinoblastoma" (national protocol)] // *Rossiyskaya pediatricheskaya oftal'mologiya [Russian Pediatric Ophthalmology].* – 2015. – №4. – P. 43–48 [in Russian];
- Kivelä T. The epidemiological challenge of the most frequent eye cancer: retinoblastoma, an issue of birth and death // *Br J Ophthalmol.* – 2009. – Vol. 93. – P. 1129–1131;
- Abramson D.H. Retinoblastoma in the 20th century: past success and future challenges – the Weisenfeld lecture // *Invest Ophthalmol Vis Sci.* – 2005. – Vol. 46(8). – P. 2683–2691;
- Brenner D., Elliston C., Hall E., Berdon W. Estimated risks of radiation-induced fatal cancer from pediatric CT // *AJR Am J Roentgenol.* – 2001. – Vol. 176(2). – P. 289–296;
- Frush D.P., Donnelly L.F., Rosen N.S. Computed tomography and radiation risks: what pediatric health care providers should know // *Pediatrics.* – 2003. – Vol. 112(4). – P. 951–957;
- Apushkin M.A., Shapiro M.J., Mafee M.F. Retinoblastoma and simulating lesions: role of imaging // *Neuroimaging Clin North Am.* – 2005. – Vol. 15. – P. 49–67;
- Schueler A.O. et al. High resolution magnetic resonance imaging of retinoblastoma // *Br J Ophthalmol.* – 2003 Mar. – Vol. 87(3). – P. 330–335;
- Chenevert T.L., Stegman L.D., Taylor J.M., Robertson P.L., Greenberg H.S., Rehemtulla A., Ross B.D. Diffusion magnetic resonance imaging: an early surrogate marker of therapeutic efficacy in brain tumors // *J Natl Cancer Inst.* – 2000. – Vol. 92. – P. 2029–2036;
- de Graaf P., Pouwels P.J., Rodjan F., Moll A.C., Imhof S.M., Knol D.L., Sanchez E., van der Valk P., Castelijns J.A. Single-shot turbo spin-echo diffusion-weighted imaging for retinoblastoma: initial experience // *AJNR Am J Neuroradiol.* – 2012. Vol. 33. – P. 110–118;
- Granata V., Fusco R., Catalano O., Guarino B., Granata F., Tatangelo F., Avallone A., Piccirillo M., Palaia R., Izzo F., Petrillo A. Intravoxel incoherent motion (IVIM) in diffusion-weighted imaging (DWI) for Hepatocellular carcinoma: correlation with histologic grade // *Oncotarget.* – 2016. – Vol. 7. – P. 79357–79364;
- Finger P.T., Khoobehi A., Ponce-Contreras M.R. et al. Three dimensional ultrasound of retinoblastoma: initial experience // *Br J Ophthalmol.* – 2002. – Vol. 86. – P. 1136–1138;
- Finger P.T., Garcia J.P.S. Jr, Schneider S. et al. "C-scan" ultrasound imaging of optic nerve extension of retinoblastoma // *Br J Ophthalmol.* – 2005. – Vol. 89(9). – P. 1225–1226;
- Yousef Y.A., Shroff M., Halliday W et al. Detection of optic nerve disease in retinoblastoma by use of spectral domain optical coherence tomography // *J AAPOS.* – 2012. – Vol. 16(5). – P. 481–483;
- Mafee M.F., Rapoport M., Karimi A, et al. Orbital and ocular imaging using 3- and 1.5-T MR imaging systems. *Neuroimaging Clin N Am.* 2005; 15(1). P. 1–21.
- Lemke A, Kazi I, Mergner U, Foerster P, Heimann H, Bechrakis N, et al. Retinoblastoma – MR appearance using a surface coil in comparison with histopathological results // *Eur Radiol.* – 2007. – Vol. 17. – P. 49–60;
- Schueler AO, Hosten N, Bechrakis NE, Lemke AJ, Foerster P, Felix R, et al. High resolution magnetic resonance imaging of retinoblastoma // *Br J Ophthalmol.* – 2003. – Vol. 87. – P. 330–335;
- Galluzzi P., Hadjistilianou T., Cerase A., De Francesco S., Toti P., Venturi C. Is CT still useful in the study protocol of retinoblastoma? // *AJNR Am J Neuroradiol.* – 2009. – Vol. 30. – P. 1760–1765;
- Saket R.R., Mafee M.F. Anterior-segment retinoblastoma mimicking pseudoinflammatory angle-closure glaucoma: review of the literature and the important role of imaging // *AJNR Am J Neuroradiol.* – 2009. – Vol. 30. – P. 1607–1609;
- de Graaf P., van der Valk P., Moll A., Imhof S., Schoutenvan A., Meeteren V. et al. Contrast-enhancement of the anterior eye segment in patients with retinoblastoma: correlation between clinical, MR imaging, and histopathologic findings // *AJNR Am J Neuroradiol.* – 2010. – Vol. 31. – P. 237–245;
- Galluzzi P., Cerase A., Hadjistilianou T., De Francesco S., Toti P., Vallone I. et al. Retinoblastoma: abnormal gadolinium enhancement of anterior segment of eyes at MR imaging with clinical and histopathologic correlation // *Radiology.* – 2003. Vol. 228. – P. 683–690;
- de Graaf P, Knol D, Moll A, Imhof S, Schouten-van Meeteren A, Castelijns J. Eye size in retinoblastoma: MR imaging measurements in normal and affected eyes // *Radiology.* – 2007. – Vol. 244. – P. 273–280;
- O'Brien J. Retinoblastoma: clinical presentation and the role of neuroimaging // *AJNR Am J Neuroradiol.* – 2001. – Vol. 22. – P. 426–428;
- Shuxian Chen et al. The value of MRI in evaluating the efficacy and complications with the treatment of intra-arterial chemotherapy for retinoblastoma // *Oncotarget.* – 2017, Jun 13. – Vol. 8(24). – P. 38413–38425;
- Broadus E., Topham A., Singh A.D. Survival with retinoblastoma in the USA: 1975-2004 // *Br J Ophthalmol.* – 2009. – P. 24–27.