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Whole-body MRI capacity in diagnostics, staging, and assessment of treatment efficiency of lymphomas: a literature review

Relevance. *Lymphomas make up to 5-6% of all malignant neoplasms in adults and up to 10% of oncological diseases in children. Due to a quite favorable overall prognosis in early detection of lymphomas, the prevention of long-term complications associated with their therapy and diagnostics remains relevant and acute. Radiological methods (CT, PET/CT 18-FDG, MRI) play an important role in the initial staging of lymphomas, the assessment of treatment efficiency and the detection of recurrences. During treatment and subsequent dynamic control, the patients with malignant lymphomas undergo multiple cycles of CT and PET-CT studies thus accumulating quite a high dose of ionizing radiation, even in the case of low-dose CT, which may contribute to an increased risk of secondary tumors in the future. It increases the interest in MRI as a radiation-free method of the staging of malignant lymphomas and dynamic observation during treatment, an alternative to CT and/or PET.*

The purpose of the study *was to assess the capacity of whole-body MRI in diagnosing, staging, and assessment of the efficiency of lymphoma treatment.*

Results. *Whole-body MRI is a highly sensitive method of primary staging and assessment of treatment efficiency of malignant lymphomas, as the efficiency of conventional MRI in malignant lymphomas is equal to CT with contrast enhancement. Moreover, MRI using DWI mode is highly comparable with the results obtained by PET/CT–18FDG and is an excellent alternative for patients with lymphomas as it is free of ionizing radiation and intravenous contrasting.*

Conclusion. *The obtained results give reason to consider MRI as a method having an identical capacity with CT and PET/CT in diagnosing, staging and assessment of the efficiency of lymphoma treatment.*

Keywords: *whole-body MRI, lymphoma.*

Introduction. Lymphomas are the tumors originating from lymphoid tissue located outside the bone marrow [1]. Lymphomas account for 5-6% of all malignancies in adults, and up to 10% of cancer diseases in children [2]. Malignant lymphoma is the most common primary hematopoietic malignant tumor, as well as one of the most treatable forms of cancer. The two main categories of lymphomas include Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). The exact initial diagnostics of lymphoma is decisive for proper treatment planning and prognosis. Radiology methods (CT, PET-CT with F-18, MRI) play an important role in the initial staging of lymphomas, evaluating the effectiveness of therapy and detecting recurrence of the disease [3-8].

Materials and Methods. The conducted literature search was conducted on the PubMed database for the last 15 years (2003-2018) by keywords «Whole-body MRI, Lymphoma». This literature review includes 30 literature sources matching the selection criteria – these are full-text scientific articles containing the analysis of whole-body MRI results in lymphomas in comparison with other methods of radiation diagnosis, such as CT and PET-CT.

Literature review. CT is the most widely used radiology method for lymphoma staging due to its wide availability and a relatively low cost. Main CT-criterion indicating the lesion of lymph nodes is the change in their size. Pathologically changed lymph nodes are longer than 15 mm and/or wider than 10 mm [9, 10]. Total sensitivity and specificity of CT at node lesions above 15 mm in size reaches 87.5 and 85.6%, respectively [10-12]. It should be noted that the main limitation for the initial staging of malignant lymphomas using CT is the low level of informativity of this method with nodal lesions smaller than 10-15 mm in size. It increases the probability of false positive conclusions in case of a benign lymph nodes' hyperplasia and lymphadenopathies of another genesis in children [13].

In lymphomas, morphological changes can fall significantly behind rapid functional changes; therefore, CT is not an ideal diagnostic tool in assessing early response to systemic therapy [8, 9, 10, 12]. In addition, CT is not applicable to the re-staging of lymphoma after completion of a course of treatment due to low informativity of this method in defining persisting viable tumor cells in large residual tumor masses [9, 11, 12]. PET-CT with F-18 is based on the fixation of positron decay of radiopharmaceutical drug which actively accumulates in foci with increased glucose consumption. Any foci with increased F-18 consumption in relation to the background tissue in the absence of benign hypermetabolic disorders is considered positive for malignant lymphoma. A meta-analysis of several prospective studies has shown that PET sensitivity and specificity in the staging of malignant lymphomas and the assessment of their response to treatment leave behind the sensitivity and specificity of contrast CT [14, 15]. The main factor defining the intensity of 18F accumulation in a tumor is the histological type of the tumor. HL and aggres-

sive types of NHL are known for their high level of glycolysis that means a high intensity of the drug accumulation in tumor foci. Moderate and low levels of glycolysis and the relevant low intensity of 18F accumulation in the tumor tissue are typical for indolent NHL. PET is an efficient method for detecting a lymphomatous lesion regardless of its size, as well as to detect active tumor cells in the residual tumor masses after completion of the course of treatment [14, 16, 17]. Several large-scale studies have proven PET-CT to be a more accurate method of staging and re-staging of malignant lymphomas than contrast CT [18, 19].

A disadvantage of PET, and especially PET-CT, is their relatively high cost that makes both methods most costly in radiation examination [20].

During treatment and future dynamic follow-up, patients with malignant lymphomas have to undergo multiple cycles of CT and PET-CT examinations. As a result, they accumulate a significant dose of ionizing radiation, even in case of a low-dose CT. It can promote the risk of secondary tumors in the future [6-8, 10]. These reasons raise interest in MRI as an option without radiation burden. MRI creates an alternative to CT and/or PET for the staging of malignant lymphomas and dynamic follow-up during treatment [10, 21]. The main advantage of the whole-body MRI is the possibility to obtain a whole picture of the pathological process spread in the body (lesions of lymph nodes of bone marrow and other organs) within one examination. Recent studies show that the whole-body non-contrast MRI protocols including diffuse-weighted images (DWI) can be used for the initial staging of lymphomas [7, 22-28]. Magnetic resonance diffusion is a method that allows determining the translational movement of intracellular water molecules in the tissues. DWI MRI has high potential in assessing malignant lymphomas. Quantitative measurement of the degree of diffusion (according to the distribution maps of the true or apparent diffusion coefficient (ADC)) can help distinguish malignant and benign lymph nodes [5, 8, 24-28]. In staging of malignant lymphomas, DWI is a valuable addition to the standard MRI protocols. DWI allows visualizing and measuring of the extra-, intra-and transcellular movement of water molecules due to their intrinsic thermal energy. The degree of freedom of movement of water molecules depends on several characteristics of the tissue such as cell packing density, the number of water molecules in the extracellular space, the concentration of protein and peptide molecules, the viscosity of the medium, and the presence of tissue necrosis. Limited diffusion is characteristic for most malignant tumors including malignant lymphomas. The use of DWI allows obtaining high contrast between the lesion focus and the background tissues which facilitates the detection of pathological foci [24-29]. Starting from 2008, many publications were devoted to incomplete and small studies of the results of using whole-body MRI for lymphomas. According to preliminary data, MRI sensitivity and specificity in detecting node lesions in malignant lymphomas reach 98-99%, in extra-node lesions – 91-99%. According to preliminary results of a range of incomplete studies, DWI can be potentially used (analog to PET) to differentiate clusters of viable tumor cells from foci of fibrosis or necrosis in tumor masses remaining after treatment [20].

Conclusions. A quite positive general prognosis at early detection of lymphomas actualizes the topic of prevention of long-term complications related to the conducted therapeutic and diagnostic procedures. All modern methods of anatomical visualization (Ultrasound, CT, and MRI) have a limited capacity of detecting metastases as they mainly rely on low-sensitive "size-anatomical" criteria. A hybrid PET-CT has high diagnostic accuracy and is gaining popularity as a method of visualization, initial staging, and assessment of evaluating the efficacy of treatment of aggressive malignant lymphomas. CT and PET-CT currently used to diagnose lymphomas are associated with exposure to significant ionizing radiation therefore attempts shall be made to reduce the exposure rate. Whole-body MRI and DWI (especially, with ADC) seem to be an effective alternative to CT and PET. A direct comparison of DWI and PET results is required to define if functional information obtained from DWI can replace PET. MRI can be especially useful for certain groups of patients like children, pregnant women, individuals with increased risk of complications from the administration of contrast agents. Moreover, MRI can become a method of choice for patients with an F-18 negative lymphoma. The value of diffuse-weighted MRI and ADC is not yet established finally. Today, PET is still required to evaluate the response to treatment. Whole-body MRI, being a relatively new radiation-free method of initial staging and evaluation of response to treatment in malignant lymphomas, becomes a widely available diagnostic option. Complex use of routine MRI with DWI and ADC can significantly increase the accuracy of diagnosis and is the subject of ongoing research.

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