Claims

1. Use of a deuterated derivative of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salt, or a mixture of at least two different deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts, in the manufacture of a diagnostic agent for use in diagnosing oncological diseases by magnetic resonance imaging and/or magnetic resonance spectroscopy at the frequency of deuterium, wherein the deuterated derivative is defined as a compound containing deuterium bound to carbon in an amount exceeding its natural amount in at least one position.
2. Use according to the claim 1, wherein the diagnostic agent further includes at least one pharmaceutically acceptable auxiliary substance.
3. Use according to the claim 2, wherein the pharmaceutically acceptable auxiliary substance is a carrier, filler and/or solvent.
4. Use according to the claim 1, wherein the deuterated derivative of 2-amino-2-methylpropionic acid is 2-amino-2-(CD_3)-3,3,3-D_3-propionic acid or 2-amino-2-(CD_2H)-3,3,3-D_3-propionic acid or 2-amino-2-(CDH_2)-3,3,3-D_3-propionic acid or 2-amino-2-methyl-3,3,3-D_3- propionic acid or 2-amino-2-(CD_2H)-3,3-D_2-propionic acid or 2-amino-2-(CDH_2)-3,3-D_2-propionic acid or 2-amino-2-methyl-3,3-D_2-propionic acid or 2-amino-2-(CDH_2)-3-D-propionic acid or 2-amino-2-methyl-3-D-propionic acid.
5. Use according to the claim 1, wherein deuterated derivative of 2-(N-methylamino)-2-methylpropionic acid is a 2-methylamino-2-(CD_3)-3,3,3-D_3-propionic acid or 2-(N-(CD_3)amino)-2-methylpropionic acid or 2-(N-(CD_3)amino)-2-(CD_3)-3,3,3-D_3-propionic acid.
6. Use according to the claim 1, wherein the diagnostic agent comprises a mixture of at least two different deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid selected from 2-amino-2-(CD_3)-3,3,3-D_3-propionic acid and/or 2-amino-2-(CD_2H)-3,3,3-D_3-propionic acid and/or 2-amino-2-(CD_2H)-3,3,3-D_3-propionic acid and/or 2-amino-2-methyl-3,3,3-D_3-propionic acid and/or 2-amino-2-(CD_2H)-3,3-D_2-propionic acid and/or 2-amino-2-(CDH_2)-3,3-D_2-propionic acid and/or 2-amino-2-methyl-3,3-D_2-propionic acid and/or 2-amino-2-(CDH_2)-3-D-propionic acid or 2-amino-2-methyl-3-D-propionic acid and/or 2-methylamino-2-(CD_3)-3,3,3-D_3-propionic acid and/or 2-(N-(CD_3)amino)-2-methylpropionic acid and/or 2-(N-(CD_3)amino)-2-(CD_3)-3,3,3-D_3-propionic acid.
7. Use according to the claim 1, wherein the diagnostic agent additionally includes non-deuterated 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid.

8. Use according to the claim 1, in which a deuterated derivative of 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salt besides the deuterium atoms attached to the carbon atoms contains deuterium atoms that partially or completely substitute dissociable hydrogen atoms attached to oxygen and/or nitrogen atoms.

9. The use according to any one of the preceding claims, wherein the mixture of at least two different deuterated derivatives is a mixture of compounds containing deuterium in different positions of the molecule, or containing different amounts of deuterium in the same position.

10. The use according to any one of the preceding claims, wherein the oncological disease is breast cancer or glioma.

~~9.~~11. The use according to any one of the preceding claims, wherein the diagnosis agent is to be administered to a subject, wherein the magnetic resonance imaging and/or magnetic resonance spectroscopy is carried out at a frequency of deuterium nuclei after administration of the diagnostic agent after a time sufficient for its accumulation in tumor tissue, for obtaining, respectively a MR image and/or a NMR spectrum, wherein the presence and absence of an oncological disease is determined based on the observed signal intensity of the deuterium nuclei, reflecting the level of accumulation of the diagnostic agent.~~A method for diagnosing an oncological disease, comprising the following stages:~~

~~a) a diagnostic agent, including a deuterated derivative of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salt, or a mixture of at least two different deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts, is administered to a subject;~~

~~b) the magnetic resonance imaging and/or magnetic resonance spectroscopy is carried out at the frequency of deuterium nuclei after administration of the diagnostic agent after a time sufficient for its accumulation in tumor tissue, for obtaining, respectively, a MR image and/or a NMR spectrum;~~

~~c) the presence or absence of an oncological disease is diagnosed based on the observed signal intensity of the deuterium nuclei, reflecting the level of accumulation of the diagnostic agent.~~

~~10. The method according to the claim 9, where in case of absence of accumulation regions of the diagnostic agent a subject is diagnosed with the absence of cancer.~~

~~11.~~12. The use ~~method~~ according to the claim 11~~9~~, wherein the subject undergoes at least one additional medical study, selected from magnetic resonance imaging at the frequency of nuclei differing from deuterium, or ultrasound, or computed tomography,

or X-ray, or palpation, or biopsy, or screening of biological materials for tumor markers, or radionuclide diagnosis or physical examination ~~is carried out~~.

~~12.~~13. The use ~~method~~ according to the claim 11~~9~~, wherein ~~which diagnoses~~ the presence or absence of an oncological disease is determined based on

(a) a ~~the~~ comparison of a signal intensity of the deuterium nuclei in the ~~examined~~ subject with a typical intensity of the signal observed in healthy subjects in the corresponding tissue or organ;~~.~~

~~13. The method according to the claim 11, which diagnoses the presence or absence of an oncological disease based on~~ (b) a ~~the~~ comparison of signal intensity of the deuterium nuclei in the regions corresponding to normal and pathological tissues according to an additional medical study;~~.~~

~~14. The method according to the claim 11, which diagnoses the presence or absence of an oncological disease based on~~ (c) a ~~the~~ comparison of a signal intensity of the deuterium nuclei in the neighboring voxels that are located at different sides of the interface between the normal tissue and the tissue suspicious for a tumor according to ^{1}H MRI; or~~.~~

~~15. The method according to the claim 11, which diagnoses the presence or absence of an oncological disease based on~~ (d) a comparison of deuterium images with the 1H magnetic resonance images from the same subject.

~~16.~~14. The use ~~method~~ according to the claim 11~~9~~, where the signal intensity of the deuterium nuclei ~~signal~~ and/or its change in time allows ~~to make~~ a conclusion to be made on the structure, malignancy grade, aggressiveness, or degree of differentiation of the tumor.

~~17. The method according to the claim 9, wherein the oncological disease is breast cancer, glioma.~~

~~18.~~15. The use ~~method~~ according to the claim 11~~9~~, wherein the magnetic resonance imaging and/or magnetic resonance spectroscopy is carried out using ~~during the registration of the image the~~ a selective excitation of deuterium nuclei included in the deuterated derivative of 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid and/or of its pharmaceutically acceptable salts, or of a mixture of deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts ~~is used~~.

~~19.~~16. The use ~~method~~ according to ~~the~~ claim 11~~9~~, wherein the magnetic resonance imaging and/or magnetic resonance spectroscopy is carried out using ~~during the registration of the image the~~ a broadband excitation of the deuterium nuclei included in the deuterated derivative of 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-

methylpropionic acid and/or of its pharmaceutically acceptable salts, or of a mixture of deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts ~~is used~~.

~~20.~~17. The use ~~method~~ according to ~~the~~ claim 11~~9~~, wherein the diagnostic agent is to be administered to a subject orally.

~~21.~~18. The use ~~method~~ according to ~~the~~ claim 11~~9~~, wherein the diagnostic agent is to be administered to a subject parenterally.

~~22.~~19. The use ~~method~~ according to ~~the~~ claim 11~~9~~, wherein~~in which~~ the magnetic resonance imaging ~~tomography~~ and/or magnetic resonance spectroscopy on the deuterium nuclei is carried out in 20-360 minutes after the administration of the diagnostic agent.

~~23.~~20. The use ~~method~~ according to the ~~claim~~ 11~~9~~, wherein the diagnostic agent is to be administered to the ~~a~~ subject in an amount corresponding to 0.25-1 g of deuterated derivative of 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts, or mixtures deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salt per 1 kg of body weight of the ~~a~~ subject.

21. A method of imaging a region of suspected malignancy in a subject using a diagnostic agent, comprising the following stages:

a) a diagnostic agent, including a deuterated derivative of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salt, or a mixture of at least two different deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts, is to be administered to the subject;

b) the magnetic resonance imaging and/or magnetic resonance spectroscopy is carried out at the frequency of deuterium nuclei after administration of the diagnostic agent after a time sufficient for its accumulation in the region of suspected malignancy including tissue suspicious for a tumor, for obtaining, respectively, a MR image and/or a NMR spectrum to acquire imaging data including a signal intensity of the deuterium nuclei, the signal intensity reflecting the level of accumulation of the diagnostic agent.

22. The method according to the claim 21, where the signal intensity of the deuterium nuclei and/or its change in time are acquired.

23. The method according to the claim 21, wherein during the registration of the image the selective excitation of deuterium nuclei included in the deuterated derivative of 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid and/or of its pharmaceutically acceptable salts, or of a mixture of deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts is used.

24. The method according to the claim 21, wherein during the registration of the image the broadband excitation of the deuterium nuclei included in the deuterated derivative of 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid and/or of its pharmaceutically acceptable salts, or of a mixture of deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts is used.

25. The method according to the claim 21, wherein the diagnostic agent is to be administered to a subject orally.

26. The method according to the claim 21, wherein the diagnostic agent is to be administered to a subject parenterally.

27. The method according to the claim 21, in which the magnetic resonance tomography and/or magnetic resonance spectroscopy on the deuterium nuclei is carried out in 20-360 minutes after the administration of the diagnostic agent.

28. The method according to the claim 21, wherein the diagnostic agent is to be administered to the subject in an amount corresponding to 0.25-1 g of deuterated derivative of 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts, or mixtures deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salt per 1 kg of body weight of the subject.

Abstract

Preparation for magnetic resonance diagnostics for oncological diseases, comprising deuterated 2-amino-2-methylpropionic acid and/or 2-(n-methylamino)-2-methylpropionic acid, and diagnostic method using said preparation

The invention relates to medicine, namely to the means for magnetic resonance imaging of the oncological diseases. For this purpose, the diagnostic agent and the diagnostic method based on the use of the diagnostic agent is developed, which is based on a deuterated derivative 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salt, or a mixture of at least two different deuterated derivatives of 2-amino-2-methylpropionic acid and/or 2-(N-methylamino)-2-methylpropionic acid and/or its pharmaceutically acceptable salts. The method of the invention involves performing magnetic resonance imaging and/or magnetic resonance spectroscopy at the frequency of deuterium nuclei after administration of the diagnostic medication after a time sufficient for the accumulation of the diagnostic agent in the tumor of a subject, for obtaining, respectively, MR images and/or MR spectra.

The proposed method allows diagnosing oncological diseases with high informational content.

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