the latter, it allows to eliminate the risks associated with ionizing radiation of the radiopharmaceutical agents.

The present invention concerns the development of a diagnostic agent that includes 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 salt, for the diagnosis of oncological diseases by magnetic resonance imaging and/or magnetic resonance spectroscopy at the frequency of deuterium nuclei.

In particular embodiments of the invention, the diagnostic agent additionally includes at least one additional pharmaceutically acceptable component. In particular embodiments of the invention pharmaceutically acceptable component is a carrier, filler and/or solvent.

In particular embodiments of the invention the deuterated derivative of 2-amino-2-methylpropionic acid is a 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.

In particular embodiments of the invention the deuterated derivative of 2-(N-methylamino)-2-methylpropionic acid is 2-(N-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.

In the other particular embodiments of the invention, the diagnostic agent is 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.

In particular embodiments of the invention, the diagnostic agent of the invention optionally includes non-deuterated 2-amino-2-methylpropionic acid or 2-(N-methylamino)-2-methylpropionic acid.

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.
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. 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. The method according to the claim 9, wherein 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. The method according to the claim 9, which diagnoses the presence or absence of an oncological disease based on 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 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 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.

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

16. The method according to the claim 9, where the intensity of the deuterium signal and/or its change in time allows to make a conclusion 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. The method according to the claim 9, 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.

19. The method according to the claim 9, 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.

20. The method according to the claim 9, wherein the diagnostic agent is administered to a subject orally.

21. The method according to the claim 9, wherein the diagnostic agent is administered to a subject parenterally.

22. The method according to the claim 9, 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.

23. The method according to the claim 9, wherein the diagnostic agent is administered to 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 a subject.