microspheres is around 17 wt.% (w/w) (Nijsen *et al.*, *Biomaterials* 2001, *22* 3073-3081 and Zielhuis *et al.*, *Biomaterials* 2005, *26*, 925-932).

Microspheres with substantially higher content of lanthanide metal are disclosed in WO-A-2009/011589. In accordance with the invention disclosed therein the microspheres with high lanthanide metal content are prepared using a lanthanide metal organic compound, while no binder or only very small amounts of binder such as poly-(L)-lactic acid is used. The lanthanide ions form a complex with a number of organic molecules, such as acetylacetonate, 3,5-heptanedione, and/or 2-(acetoacetoxyethyl)methacrylate. The invention of WO-A-2009/011589 shows that the reduction of binder material does not lead to a disintegration of the microspheres. Instead, the resulting microspheres are highly stable and contain a high amount of lanthanide while no (or hardly any) binder is needed. Accordingly, microspheres having a lanthanide metal content of more than 20 wt.%, based on total microsphere, can be prepared. These microspheres have a number of advantages, including a shorter neutron activation time and higher specific activity. This in turn leads to a reduced amount of microspheres to be administered to patients and improved MRI (magnetic resonance imaging) signals.

It would, however, be desirable to design microspheres wherein the ligands complexing with the lanthanide metal are based on compounds naturally occurring in the body, so that, when applied to a patient, possible toxic effects of the microspheres are minimized.

Summary

In one aspect, there is provided a method for preparing a microsphere that comprises a lanthanide metal phosphate complex, the method comprising:

(a) providing an organic lanthanide metal complex microsphere, wherein the lanthanide metal is present in an amount of more than 20 wt.%, based on total weight of the microspheres, and wherein the organic lanthanide metal complex comprises a lanthanide ion and organic ligands with which the lanthanide ion forms the complex; and thereafter

(b) replacing at least part of the organic ligands in the organic lanthanide metal complex microsphere with phosphate in a chimie douce reaction,

wherein the lanthanide metal is present in the resulting microsphere in an amount of more than 20 wt.%, based on total weight of the microsphere, and wherein the lanthanide metal complex in the resulting microsphere comprises a lanthanide ion and phosphate.

In another aspect, there is provided a microsphere obtainable by a method as defined herein.

In yet another aspect, there is provided a microsphere comprising a lanthanide metal phosphate complex wherein the lanthanide metal is present in an amount of more than 20 wt.% based on total weight of the microsphere, and wherein the lanthanide metal complex comprises a lanthanide ion and phosphate.

In yet another aspect, there is provided a powder comprising a number of microspheres as defined herein.

In yet another aspect, there is provided a suspension comprising the microsphere as defined herein or a powder as defined herein, said suspension preferably being a therapeutic suspension, an MRI scanning suspension, and/or a nuclear scanning suspension.

In yet another aspect, there is provided the use of a microsphere as defined herein, a powder as defined herein, or a suspension as defined herein in the manufacture of a medicament for detecting and/or treating a malignancy, wherein said malignancy preferably comprises a liver metastasis.

In yet another aspect, there is provided a method for detecting a tumour, comprising

- obtaining a scanning image from an individual that had been administered the a scanning suspension as defined herein; and
- determining whether said image reveals the presence of a tumour.

In yet another aspect, there is provided a therapeutic composition comprising a microsphere as defined herein, a powder as defined herein, or a suspension as defined herein, wherein the microsphere(s) is (are) radioactive.

Detailed Description

Objective of the invention is to meet this existing need in the art and provide improved lanthanide metal microspheres.

The inventors found that this objective can, at least in part, be met by providing lanthanide metal nanospheres or microspheres wherein the lanthanide is present in a specific different complex.

In a first aspect, the invention is directed to a method for preparing a microsphere that comprises a lanthanide metal phosphate complex, the method comprising