CLAIMS

1. A method of imaging a region in a scattering medium by diffuse luminescence molecular imaging, said region comprising: at least one luminescent marker arranged in said scattering medium at a marker position, wherein said luminescent marker is a non-linear luminescent marker; the method comprising:

exciting said luminescent marker by excitation light emitted by one or more light sources into an excitation volume from at least one light source position, and

detecting luminescence from said luminescent marker due to said excitation light by a detector at a luminescent light detection position,

providing movement between said light source position and said marker position,

imaging said luminescent marker based on a non-linear dependence of said detected luminescence on said excitation light intensity and said light source position in relation to said marker position, and

calculating an excitation field from said excitation light,

calculating an emission field from said luminescent marker,

calculating a product of said excitation field according to said non-linear dependence, and

wherein said calculation of said emission field is based on said product.

2. Method according to claim 1, wherein said non-linear dependence is given by the relationship

$$L=k*E^{x},$$

wherein

E is excitation light intensity in said excitation volume

L is luminescence light intensity from said luminescent marker

k is a positive constant

x is a positive number larger than one.

3. Method according to claim 1, wherein providing said movement comprises; moving said light source position in relation to said marker position.

4. Method according to claim 1, wherein providing said movement comprises; moving said marker position in relation to said light source position.

5. Method according to claim 3, comprising;

scanning said one or more excitation beams between a plurality of said light source positions such that said light source position is moved in relation to said marker position.

6. Method according to claim 5, comprising;

detecting said luminescence for each of said plurality of light source positions, said luminescence having a total luminescence intensity of said luminescent marker for each of said plurality of light source positions,

imaging said luminescent marker by making an image of said total luminescence intensity for each of said plurality of light source positions.

7. Method according to claim 6, wherein said total luminescence intensity is provided by summing of said luminescence of said luminescent marker.

8. Method according to claim 5, wherein said plurality of light source positions forms a grid pattern, said luminescence marker having a projected area on said grid pattern.

9. Method according to claim 8, wherein said projected area is less than the area covered by said grid pattern.

10. Method according to claim 8, wherein said one or more light sources are scanned between said plurality of light source positions such that said excitation volume does substantially not overlap between two successive light source positions in said grid pattern.

11. Method according to claim 9, wherein said excitation volume is substantially localized to each of said plurality of light source positions such that said luminescent marker is partially excited if said light source position overlaps partially with said projected area.

12. Method according to any of claims 1-11, comprising exciting said luminescent marker by two or more light sources simultaneously.

13. Method according to any of claims 1-12, comprising

exciting said luminescent marker by a first light source having a first wavelength from a first light source position,

exciting said luminescent marker by a second light source having a second wavelength from a second light source position.

14. Method according to claims 13, wherein said first wavelength is substantially identical to said second wavelength.

15. Method according to claim 13, wherein said luminescent marker is excited by said first and second light sources simultaneously.

16. Method according to claim 13, wherein at least one of said first and second light source positions is moved in relation to said marker position.

17. The method of any of claims 1 - 16, wherein said diffuse luminescent imaging comprises diffuse luminescent tomography.

18. Method according to claim 17, comprising;

scanning said one or more light sources between a plurality of different light source positions such that said light source position is moved in relation to said marker position, and

detecting said luminescence for providing luminescence images of said luminescent marker for each of said plurality of different light source positions,

reconstructing a three-dimensional tomographic image of said luminescent marker from said luminescence images.

19. Method according to claim 18, wherein reconstructing said three-dimensional tomographic image comprise;

calculating an excitation field from said excitation light,

calculating an emission field from said luminescent marker,

calculating a product of said excitation field according to said non-linear dependence, and

wherein said calculation of said emission field is based on said product.

20. Method according to claim 19, wherein calculating said product comprises;

multiplying the field strength of said excitation field so as to form a product of said field strength raised to the power corresponding to the power dependence of said non-linear relationship.

21. Method according to claim 20, comprising calculating the quadratic product of said field strength.

22. Method according to claim 1, wherein providing said movement comprises moving said luminescent light detection position in relation to said marker position.

23. A system for diffuse luminescence molecular imaging of a region of interest in a scattering medium, said system comprising a luminescent marker for use in said luminescent molecular imaging of said scattering medium, wherein said luminescent marker is a non-linear luminescent marker arranged in said scattering medium, said system comprising;

one or more light sources positioned by at least one light source position for exciting said luminescent marker by excitation light emitted by said one or more light sources into an excitation volume,

a detector at a luminescent light detection position detecting luminescence from said luminescent marker due to said excitation light, wherein said luminescent molecular imaging comprises imaging said luminescent marker based on a non-linear dependence of said detected luminescence on said excitation light intensity and said light source position in relation to said marker position, and calculating an excitation field from said excitation light,

calculating an emission field from said luminescent marker,

calculating a product of said excitation field according to said non-linear dependence, and wherein said calculation of said emission field is based on said product.

24. The system of claim 23, wherein said luminescent marker is comprised in a group of non-linear luminescent markers configured to upconvert incoming light of an illumination wavelength, such that luminescence occurs at a luminescence wavelength that is shorter than said illumination wavelength when said luminescent marker is illuminated with said incoming light.

25. The system of claim 23 or 24, wherein said luminescent marker is a luminescent biological marker, and said scattering medium is tissue of a human or animal, said luminescent biological marker being arranged in said tissue.

26. The system of any of claims 23 to 25, wherein said luminescent marker comprises nanosized upconverting particles.

27. The system of claim 26, wherein said nanosized upconverting particles are of sodium yttrium tetrafluoride ($NaYF_4$), co-doped with either Yb^{3+}/Er^{3+} or Yb^{3+}/Tm^{3+}.

28. The system of claims 23 to 26, wherein said non-linear luminescent marker comprises particles that are water soluble.

29. The system of claim 28, wherein said particles are nanosized upconverting particles that are coated with a structure that is polar.

30. The system of claim 28, wherein said particles are nanosized upconverting particles having hydroxyl groups attached the surfaces of the upconverting particles

31. The system of any of claims 23 to 30, wherein said marker has a protective coating.

32. The system of any of claims 23 to 31, wherein said luminescent marker is a biological marker that is biofunctionalized.

33. The system of any of claims 23 to 32, wherein said system is devised for luminescence molecular tomography.

34. The system of any of claims 23 to 32, wherein said non-linear markers are attached to an imaging contrast agent for an imaging modality different from a modality for said luminescent imaging.

35. The system of claim 34, wherein said non-linear marker is attached to an organic gadolinium complex or gadolinium compound, which has paramagnetic properties, and wherein said system further comprises a magnetic resonance imaging (MRI) apparatus for simultaneous imaging of said region of interest by MRI and luminescence molecular tomography.

36. The system of any of claims 23 to 35, wherein said incoming light of an illumination wavelength is comprised of two or more excitation beams simultaneously.

37. System according to any of claims 23-36, wherein said excitation light is provided by a first light source having a first wavelength from a first light source position, and a second light source having a second wavelength from a second light source position.

38. System according to claim 37, wherein said excitation light is provided by said first and second light sources simultaneously.

39. Use of a system of any of claims 23 – 38 for luminescence imaging or luminescent tomography of tablets.

40. Use of a system of any of claims 23 – 38 for in-vivo or in-vitro luminescence imaging or luminescent tomography of a small animal.

41. Use of a system of any of claims 23 – 38 for functional diagnostics, such as cancer diagnostics, by said luminescence imaging or luminescent tomography.

ABSTRACT

A method and system for luminescence molecular imaging or tomography of a region of interest in a scattering medium is disclosed. The system comprises a non-linear luminescent marker material arranged in the scattering medium. Contrast and resolution of the imaging or tomography is thus improved. The non-linear marker is for instance configured to upconvert incoming light of an illumination wavelength. The non-linear power dependence of the marker enables further improvement of the imaging by using images taken with two or more excitation beams simultaneously.

Figure to be published with the abstract: Fig. 9