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Hyperintens contrast measurement and quantification of molecular probes

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1. Purpose

In this work, the MR-detectability of iron labeled microspheres is investigated and optimized by in-vitro and in-vivo experiments as well as simulations. We derive an analytical formula to quantify the dipolar field strength of localized contrast media clusters.

2. Material and Methods

The investigated microspheres have a diameter of about 0.3 mm and contain 81 ng SPIO. The z-component of their induced dipolar field is given by Eq. 1 and Eq. 2 (see below). The microspheres can potentially be used to embolise tumors or to monitor the islets-therapy. Two different hyperintens imaging methods are evaluated to optimize the detectability of the microspheres: a gradient-echo dephasing sequence, called "Whitemarker"[1], and a spectral method, called "IRON" [2]. In the Whitemarker-method, gradient moments are not balanced and hence the spins are not rephased. Near the microspheres, gradients of the dipolar field can re-balance the dephasing and the corresponding spins give high signal intensity, while the dephased undisturbed proton spins have a decreased signal. In the IRON-method, on-resonant water- and fat-protons are saturated with spectral selective inversion pulses. Then, only the disturbed off-resonant protons with a modified lamor-frequency contribute to thesignal. This sequence is spin echo (SE) -based. Susceptibility artefacts disturb the image reconstruction of the signal depending on image orientation and read-gradient strength. Series of measurements in 2% agar phantoms were taken out on a 1.5 T MAGNETOM AVANTO, Siemens Healthcare, Erlangen Germany and compared to simulations. The Whitemarker-method was tested at different dephasing states and directions. The IRON-Method was evaluated with different inversion bandwidth, inversion times, gradient strengths and imaging directions. Thereby, we tried to quantify the detectability of the microspheres by looking at the signal intensity differences. The results were than tested in-vivo on mice.

Eq. 1

$$B_{z,inh} = c\,\frac{x^2 + y^2 - 2\,z^2}{\left(x^2 + y^2 + z^2\right)^{5/2}}$$

z-Component of the magnetic dipolar field.

Eq. 2

$$c = \frac{B_0 \Delta\chi V}{4\pi}$$

Definition of the constant c in Eq. 1

We derived an analytic formula to evaluate the dipolar field strength c (see Eq.1 and 2) by using the

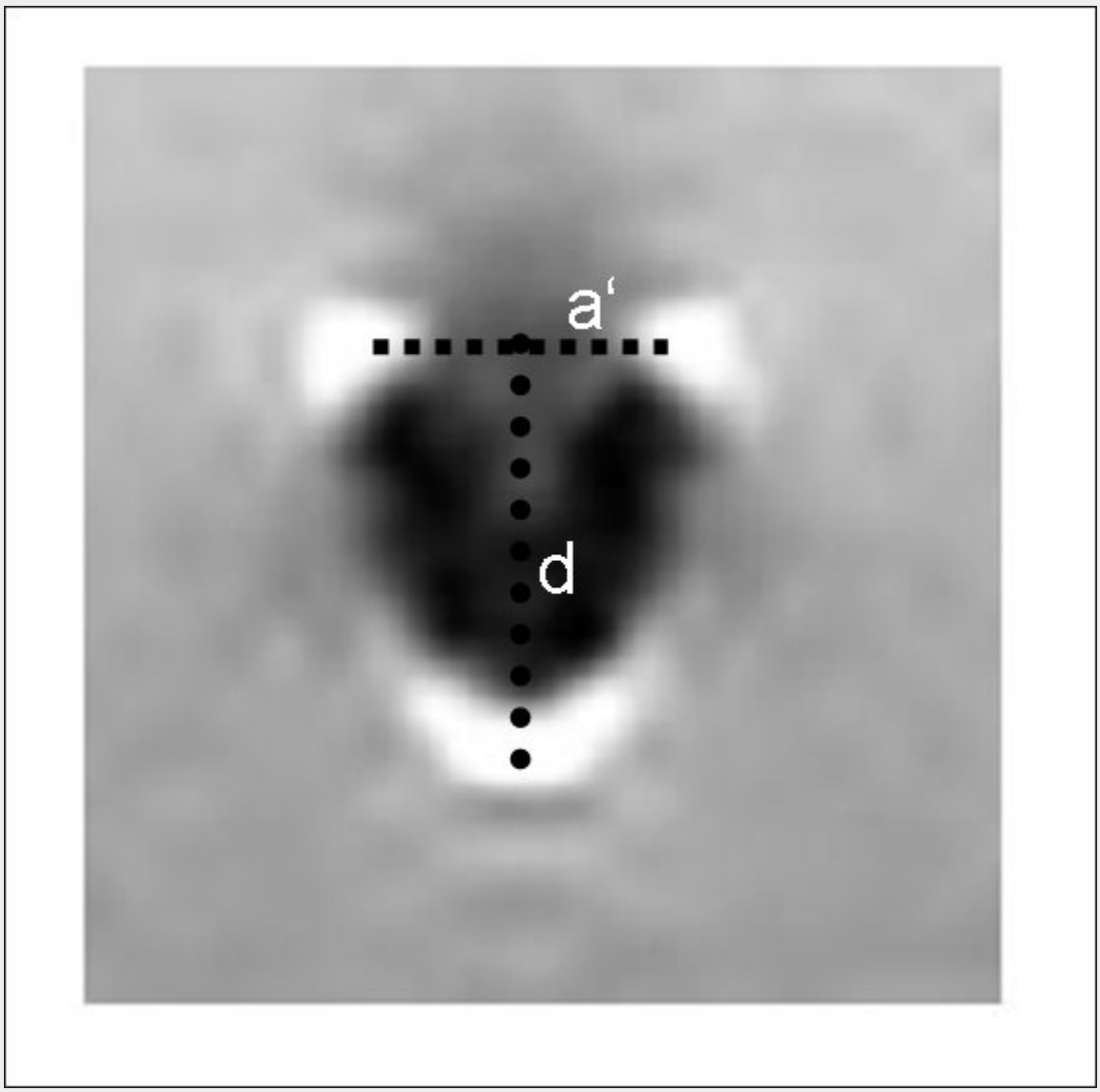
measured susceptibility artefacts in a standard SE sequence, see Eq. 3. G is the Read-Gradient. For small disturbances, distance a' is sometimes hardly measurable. In this case we found that d ≈ a'√2. This can be inserted into the formula given above and has the advantage of easier measurement, as the distance d is longer than a'.

Eq.3

$$c = \frac{3^{5/2}}{2^8} G\, a'^4 \approx 0.061\, G\, a'^4$$

Analytical derived formula to quantify the factor c in Eq. 1 and 2. G is the strengths of the read-gradient.

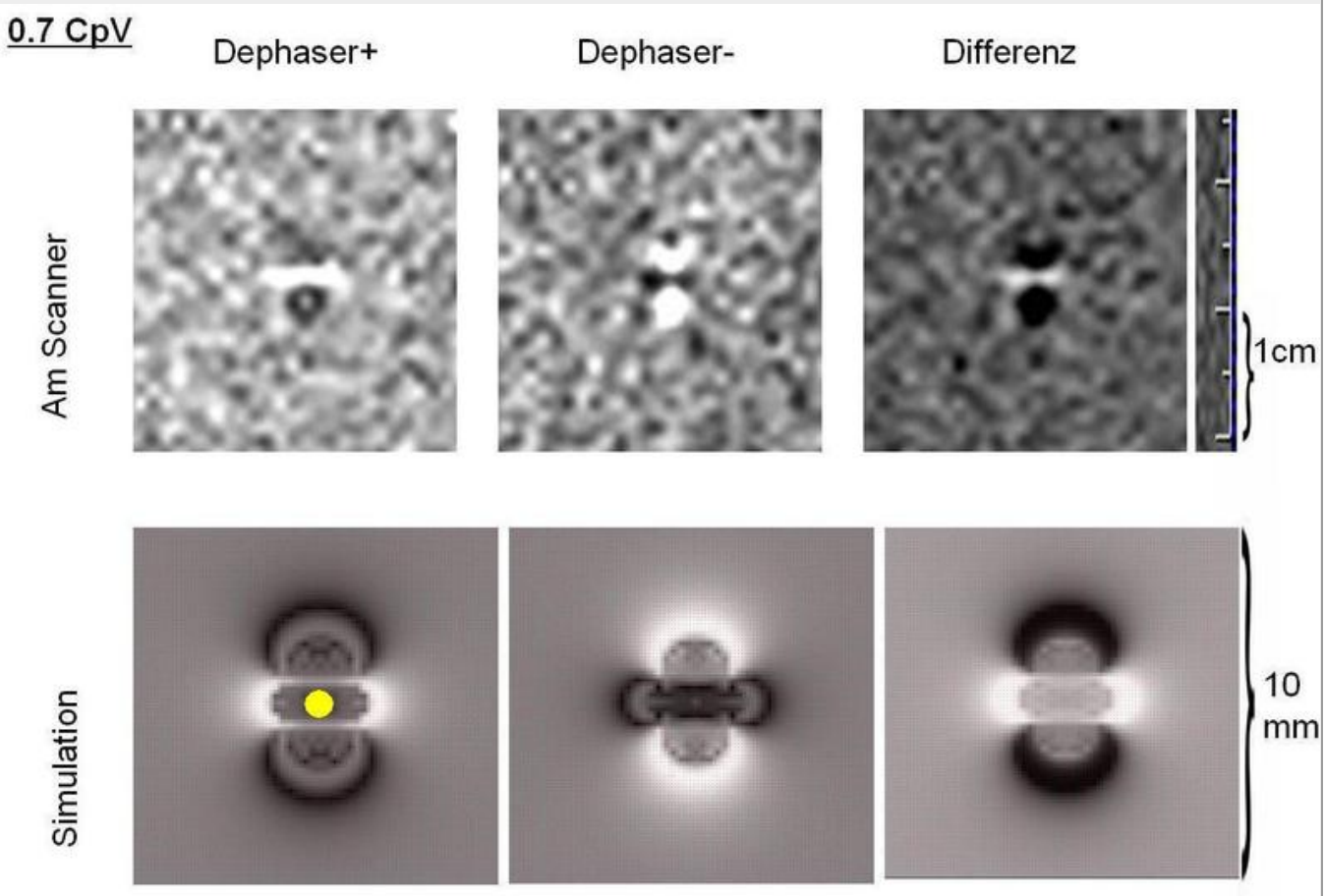
Fig 1: Susceptibility artefact



Typical shape of susceptibility artefacts in coronal and sagittal SE-Measurements.

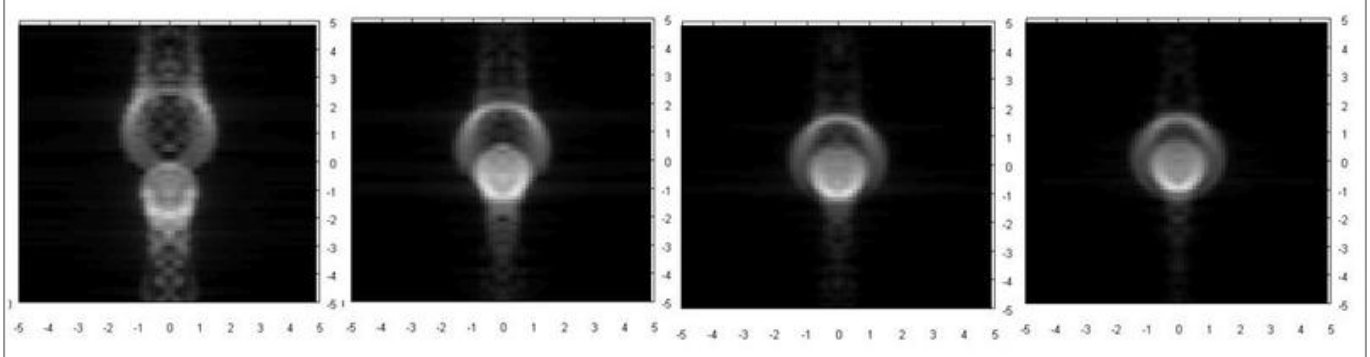
3. Results

Fig. 2



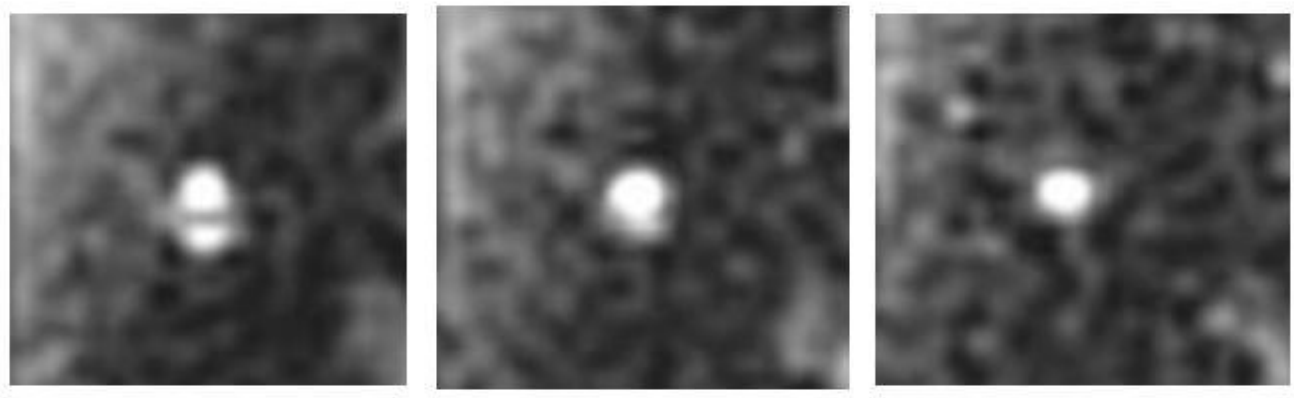
Measurement (top) and simulation (bottom) of the Whitemarker-method with a dephasing of 0.7 CpV in slice-direction. The actual size of the microspheres is drawn in the lower image on the left.

Fig. 3 (a)



Simulation of transversal IRON-Images with rising Readgradient-strengths (GRead=2.5 – 19 mT/m).

Fig. 3 (b)



Measurement of transversal IRON-Images with rising Readgradient-strengths (GRead=3-18 mT/m).

For the Whitemarker-method simulations and measurements consistently show that best detectability is reached at an intravoxel dephasing of 1.0 Cycles per Voxel (CpV) in slice-direction. For difference images of positive and negative dephasing best detectability is reached at 0.7 CpV, see Fig. 2. In case of the IRON method, best results are obtained in transversal image direction, which is explained by the z-component behaviour of the dipolar field distribution and the corresponding susceptibility artefacts. With high read gradients (>15 mT/m), susceptibility artefacts produce point-like shapes which are detected easily. This is shown in Fig. 3 a and b. In in-vivo experiments, other susceptibility effects originating from disturbances like air bubbles or tissue changes can produce simular effects and can make the microspheres hard to detect.

The derived formula to quantify the dipolar field strengths shows good match with simulated images and measured artefacts. Test measurements were done on a steel ball with a diameter of 0.5mm. An accuracy of c to a factor of 2-4 is found.

4. Conclusion

In conclusion, the spectral method has both higher detectability and resolution. However, it is limited for tissue with inhomogeneous T1 distributions. Disadvantage of both methods is the sensitivity to other magnetic disturbances. The visible effects could also be caused by other susceptibility giving defects, like air bubbles. Advanced image postprocessing could help to distinguish the source of the susceptibility artefacts.

With the derived formula, c can be calculated with a precision of half an order of magnitude. A quantitative dipolar strength measurement can be used to estimate the number of accumulated microspheres and other discrete molecular tracers in MR measurements.

5. References

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[3] K.M. Lüdeke, P. Röschmann, and R. Tischler. Susceptibility Artefacts in NMR Imaging. Magn Reson Med, 3:329-343, 1985.

6. Mediafiles

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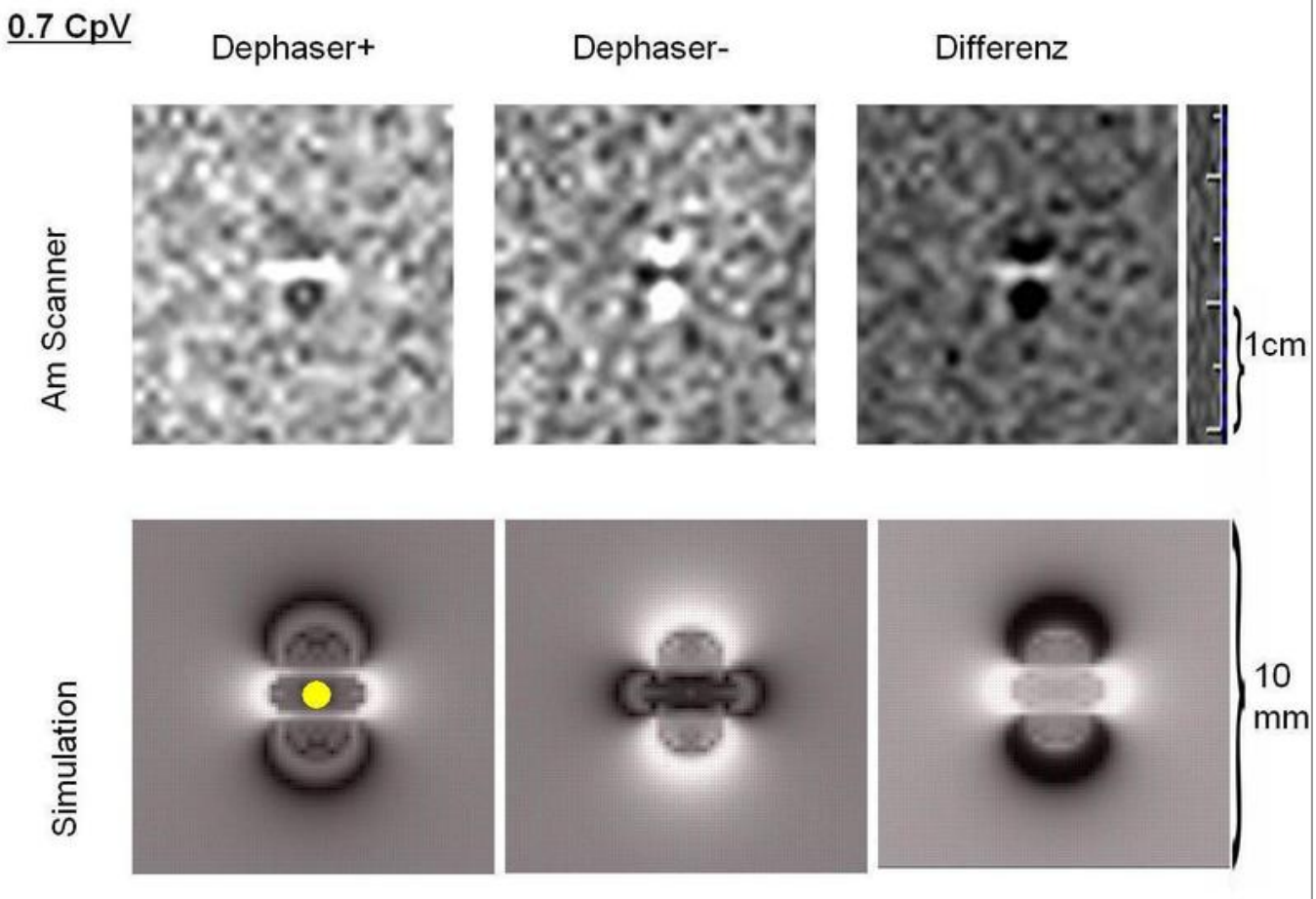

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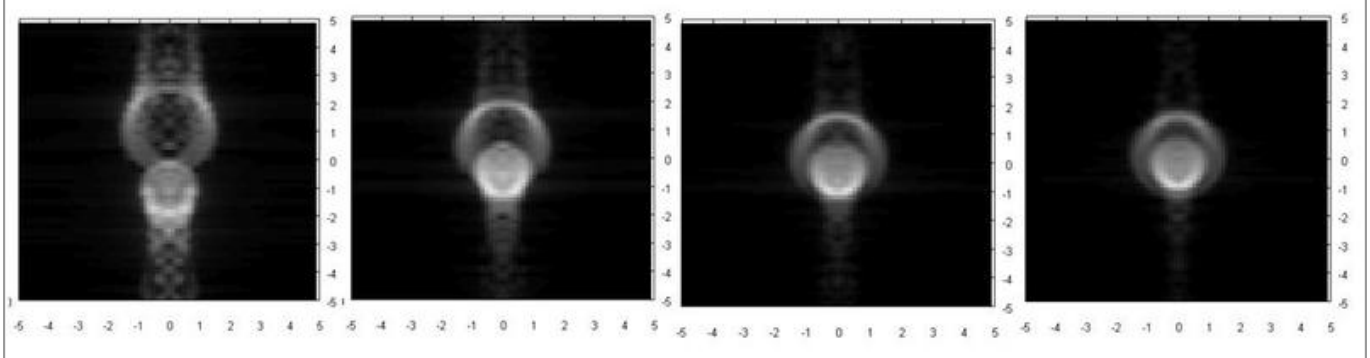

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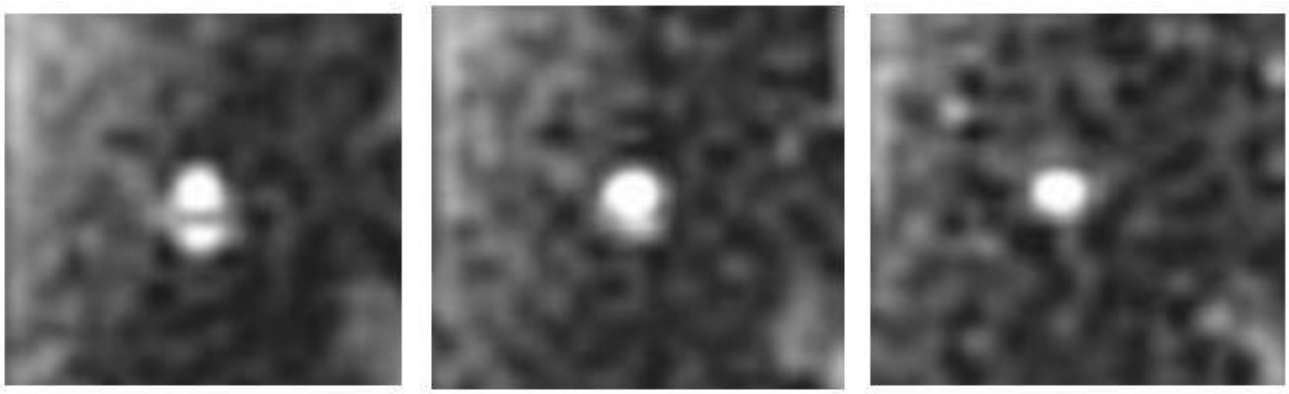

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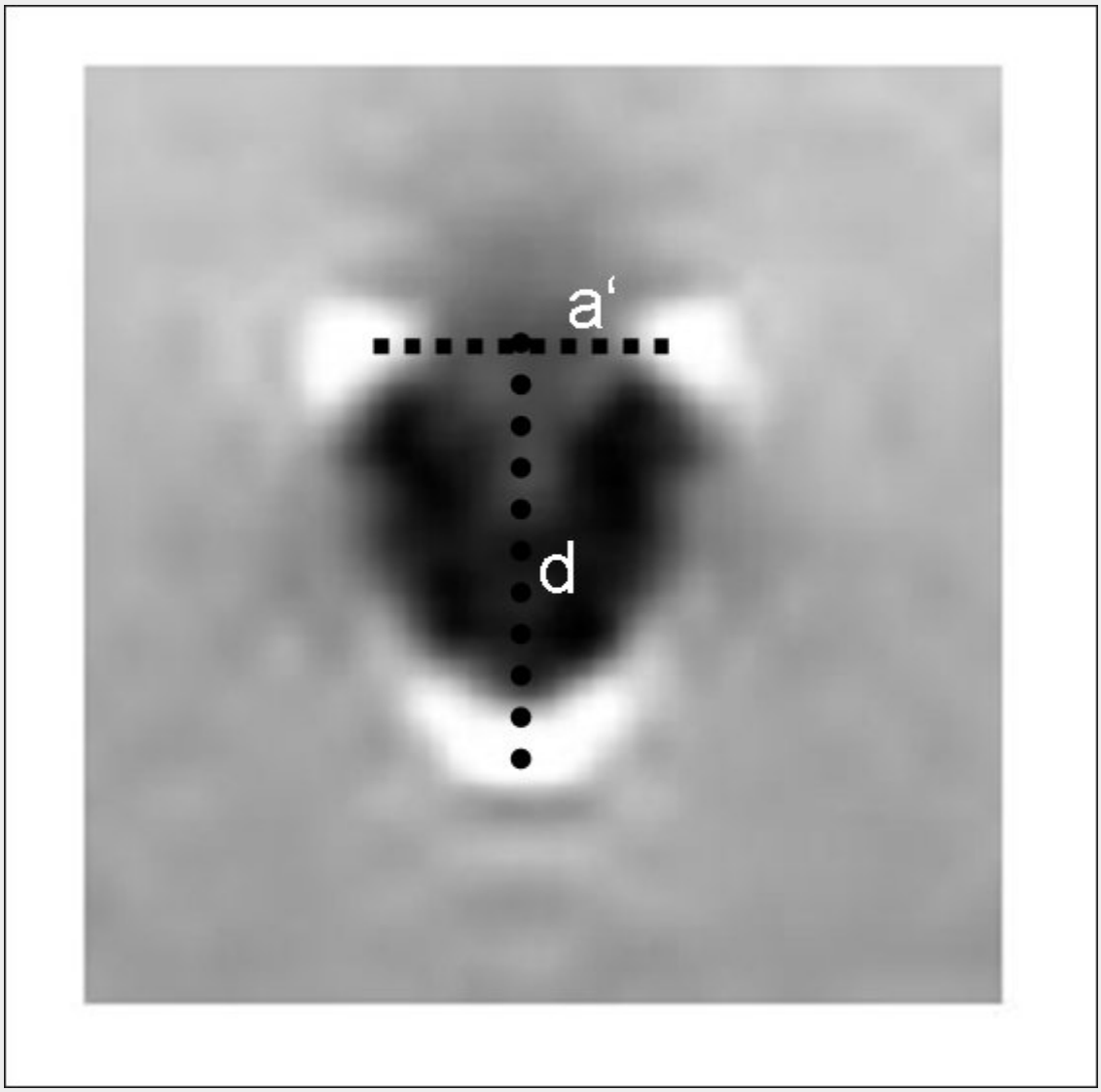

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