A complete quantification study on x-ray image contrast induced by gold nanoparticles for planar imaging and Computed Tomography at preclinical and clinical energies

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INTRODUCTION

Gold nanoparticles (GNPs) are already recognized as a promising contrast agent in planar x-ray and Computed Tomography (CT) imaging, and as drug carriers for targeted therapy [1]. In both cases, being able to determine the allocation of the GNPs *in vivo* and defining the lowest, detectable solution concentration, is of crucial importance in several applications. A complete quantification study between GNPs solution concentrations and x-ray image contrast induction has been performed and is presented for the first time.

METHODS & MATERIALS

The measurements were carried out on four x-ray imaging systems, to account for both preclinical and clinical energies (30-140 kVp). For planar imaging, a prototype bench top system, with a spatial resolution of 0.1 mm at 30 cm source to surface distance (SSD) was used, along with a planar medical system (Siemens). For CT imaging, the commercial X-CUBE™ system (Molecubes BE), having a spatial resolution of 0.05 mm was used, along with a medical CT system (Lightspeed GE). The image contrast was quantified through Contrast to Noise Ratio (CNR) [2] for planar imaging and through Hounsfield Units for CT imaging. GNPs samples (AuroVist™ 15 nm Nanoprobes) of 0.01-200 mg GNPs/ml were studied. Selected concentrations were validated through in vivo imaging.

RESULTS & DISCUSSION

Planar x-ray imaging

The imaging studies showed that for preclinical planar imaging, where an x-ray tube and a CMOS detector were used at an SSD of 30 cm, concentrations as low as 2 mg Au/ml were visible, i.e. presenting a CNR > 5. The best CNR was found for 40 kVp, thus confirming the optimal energy for x-ray imaging of GNPs at preclinical energies. For the clinical planar x-ray system, higher concentrations were required and solutions started being noticeable (CNR > 5) at around 5 mg Au/ml.

Pre-clinical Energies

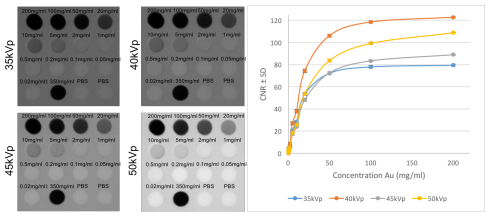

Figure 1: Quantification between GNPs concentration and x-ray contrast was based on phantom imaging studies. An example for the preclinical planar x-ray and four different energies is shown.

Clinical Energies

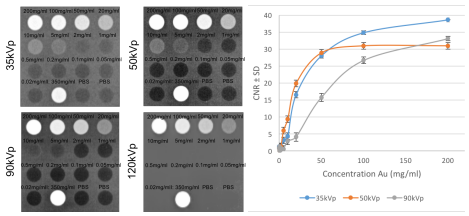

Figure 2: The quantification between GNPs concentration and x-ray contrast for a clinical radiographic system. The contrast induced by the tested concentrations for three indicative energies is shown.

Computed Tomography

CT imaging greatly improved the detection sensitivity, as expected [1]. For the clinical CT system, solutions of 0.1 mg Au/ml induced contrast values around 7 HUs and became clearly evident at 2 - 5 mgAu/ml, presenting contrast values of 70 - 150 HUs. The lowest detectable concentration was found through the X-CUBE™ system, before post processing application. Concentrations of 0.1 mg/ml and of 1 mg/ml produced values of 21 HUs and of 114 HUs, respectively. A much greater sensitivity emerging from a wider range of HUs, allowed for far better discrimination of structures.

Pre-clinical Energies

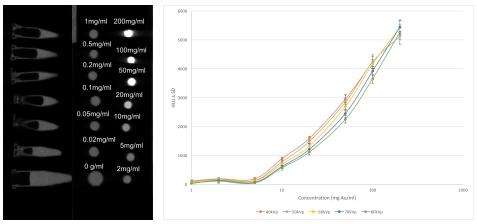

Figure 3: The phantom used for preclinical CT imaging with X-CUBE™ and the corresponding Hus ± SD for all tested concentrations. A concentration of 1 mg Au/ml produces a contrast of 114 HUs.

Clinical Energies

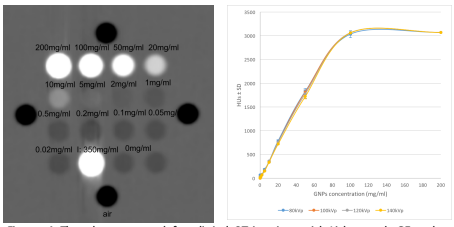

Figure 4: The phantom used for clinical CT imaging with Lightspeed GE and the corresponding HUs ± SD for tested concentrations. 2 mg/ml produce a contrast of 70 HUs, starting to be noticeable. Some artifacts and a plateau are also evident at very high concentrations of gold and iodine.

In vivo imaging studies

In vivo imaging studies were performed with the X-CUBE™ system at various energies with selected concentrations. The optimal imaging energy (optimal contrast) is showing in the following examples.

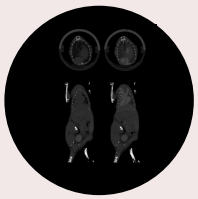

Figure 5: Pre and post contrast images of a mouse that was injected with 200 μL of 50 mg/mL solution (corresponding to 10 mg of Au in the mouse circulation, i.e. 6.7 mg/mL), acquired at 40 kV. The heart and vessels can be clearly seen without post processing. A volume of 1.5 mL of blood has been assumed.

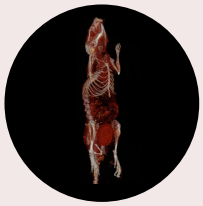

Figure 6: Bone segmentation image of a mouse injected with 200uL of 20 mg/mL solution (corresponding to 4 mg of Au in the mouse circulation, i.e. 2.7 mg/mL), acquired at 40 kV. Vessels start to appear after post processing.

Figure 7: Bone segmentation image of a mouse injected with 200uL of 50 mg/mL solution (corresponding to 10 mg of Au in the mouse circulation, i.e. 6.7 mg/mL), acquired at 40 kV. The heart and vessels can be clearly distinguished.

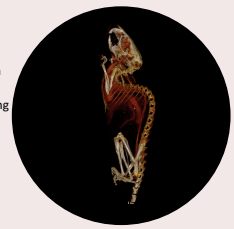

Figure 8: Bone segmentation image of a mouse injected with 200uL of 200 mg/mL solution (corresponding to 40 mg of Au in the mouse circulation, i.e. 27 mg/mL), acquired at 40 kV. Even minor vessels are very clearly distinguished.

Conclusion

A full quantification study between GNPs' (15 nm) concentration and x-ray image contrast induction has been performed, over a wide range of solutions and energies, both at preclinical and clinical level, and in planar and tomographic mode. The minimum detectable concentration has been defined for each mode and selected indicative concentrations have also been validated through *in vivo* imaging.

References

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