All that glitters is gold: towards imaging intra-arterial atherosclerosis

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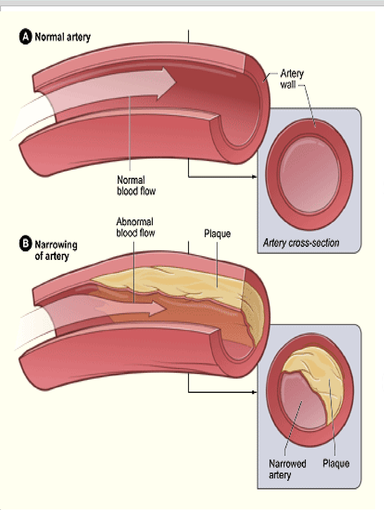
1. Context



Atherosclerosis is a disease that causes plaque - a fatty, cholesterol filled substance – to build up in the arteries. This could lead to other diseases, including coronary heart disease (the number one cause of death around the world)[1].

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Figure 1. Atherosclerotic artery. https://www.nhlbi.nih.gov/health-topics/atherosclerosis

One common imaging technique for interventional cardiology is optical coherence tomography (OCT). OCT utilizes near-IR light (wavelength about 1,300 nm) to generate tomographic images with histological-grade resolution. This enables OCT to provide intravascular assessment for thrombus, plaque morphology and stent evaluation.

OCT works by splitting light into two beams: one travels towards a reference point, and the other towards the sample. Both travel back to the splitter, recombine and travel towards a computer where an image is generated.

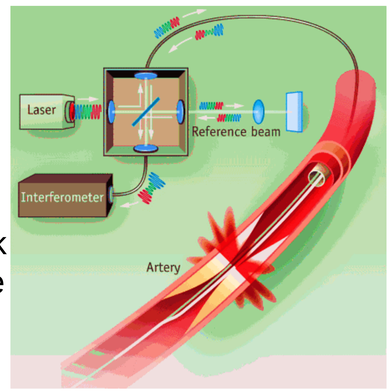


Figure 2. A diagram demonstrating the way in which OCT images are captured.

However, intracardiac OCT only provides anatomical images of the artery lumen. Molecular information, which can provide earlier diagnosis of the disease, necessitates a contrast agent..

2. Goal

To see if a contrast agent can be designed to allow for molecular OCT of atherosclerotic arteries.

3. Materials

- Gold-plated nanoparticles to provide brightness in the OCT image

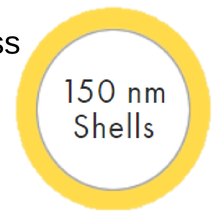
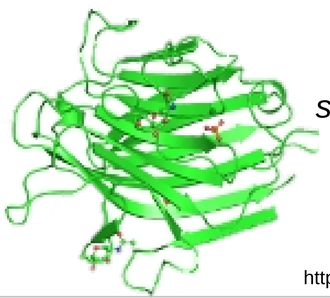


Figure 3. The nanoparticle: https://nanocomposix.com/collections/nanoshells.



- Lectin, *Griffonia simplicifolia* (conjugated to the particles to have them stick to the tissue).

Figure 4. *Griffonia simplicifolia*. https://www.bio-world.com/glycobiology/lectins.html.

4. Methodology - conjugation

In a buffer solution, the lipoic acid residues on the nanoparticles were activated with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and N-hydroxysuccinimide (NHS). Then, the lectin was added.

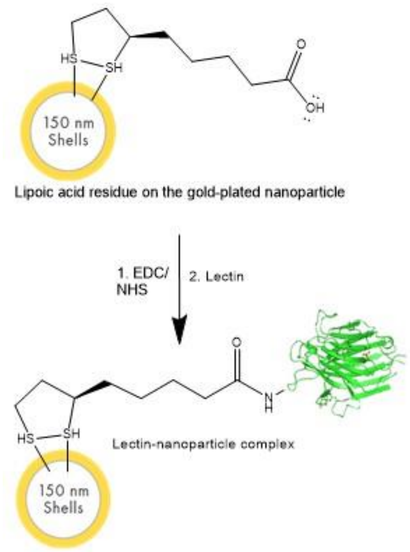


Figure 5. Reaction mechanism showing the coupling of the lectin to the nanoparticle.

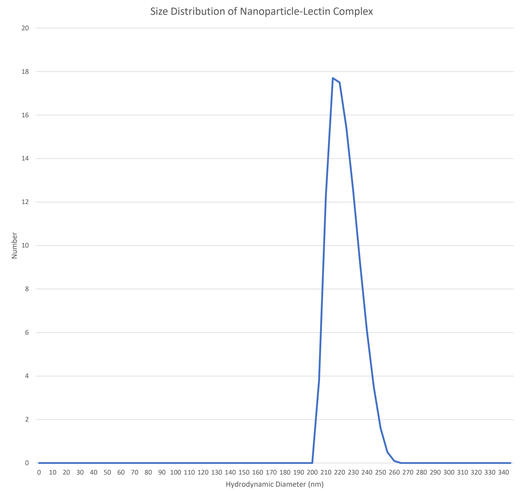


Figure 6. The number of nanoparticle-lectin molecules of a particular size, in nm.

After size analysis, most of the nanoparticles were found to be about 215 nm in diameter, with sizes ranging from 205nm to 260nm.

5. Methodology – injection and imaging

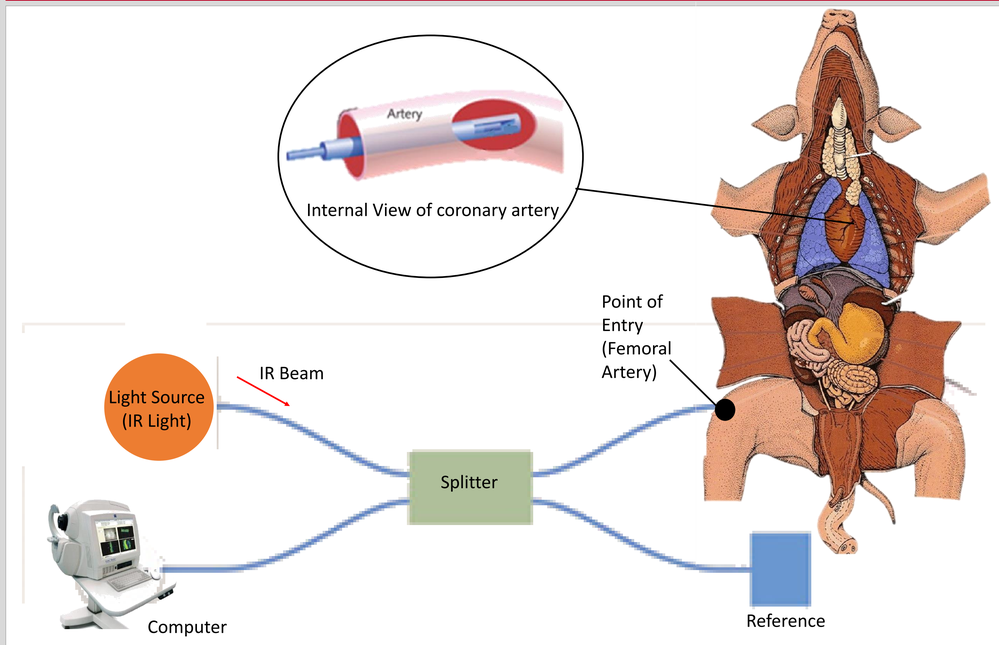


Figure 7. A diagram demonstrating the OCT setup within the pig.

As explained in the introduction, the IR wavelength split into two beams – one traveled towards the reference and back, and the other towards the sample (the coronary artery of the pig).

Briefly, the anesthetized pig underwent femoral arterial access with manual palpation and entrance via a percutaneous needle. Using the Seldinger technique, the coronary artery was accessed and a catheter was inserted. The coronary wire followed the catheter, and its placement was confirmed with fluoroscopic guidance. An intravascular OCT catheter was advanced over the coronary wire, in order to allow imaging. This was performed twice – once before and once after the implantation of a stent.

6. Results

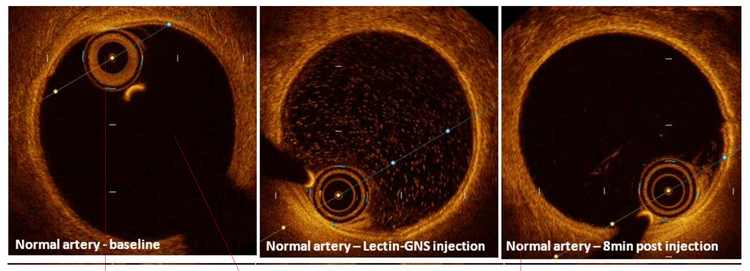


Figure 8. Results from the imaging of a normal, baseline artery.

These three images demonstrate that the contrast agent provided signal enhancement by OCT in vivo, however tissue binding was limited.

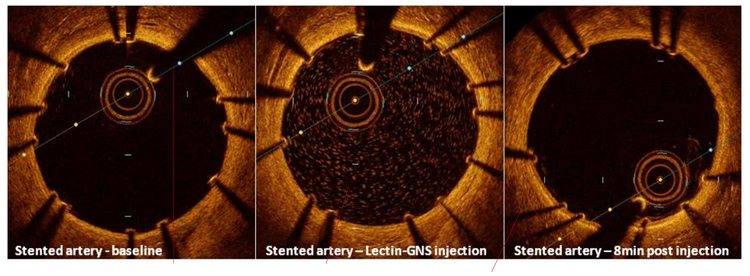


Figure 8. Results from the imaging of a stented artery.

These images were captured after the stent implantation, demonstrating again that gold nanoparticles can provide for OCT contrast – however, tissue targeting was not observed..

7. Conclusion & future significance

Firstly, the lectin and the gold nanoparticle were conjugated together, forming a complex that can both scatter light and stick to the arterial wall. This complex was then injected into the pig, and images were captured using OCT.

Despite the high quality of the images, they are not enough to see if the lectin properly binds to the tissue. This is likely because not enough time was given to let the complex circulate around the pig. Overall, the project demonstrates future potential, with some refinement.

In future studies, the contrast agent will be left to circulate longer to maximize binding potential.

9. Acknowledgements

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I would also like to thank the UROP committee for helping to fund this project, and for providing me with the opportunity to learn about research.

10. Sources

1. http://www.who.int/mediacentre/factsheets/fs317/en/

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