Synthesis of Gold Modified Silica Nanotubes for OCT Imaging in Diagnosis of Diabetic Retinopathy

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ABSTRACT

With a rapid rise in diabetes and other metabolic diseases, there is an urgent medical need to develop novel diagnostic methods. A common consequence of diabetes is diabetic retinopathy, which can be detected through retinal imaging techniques such as angiography. These images can detect anatomical changes in the retina, but only after partial vision loss occurs due to diabetic retinopathy. Optical coherence tomography (OCT) is an imaging, can be used to image the retina before vision loss occurs. **Our aim is to synthesize gold-coated silica nanotubes to detect changes in the retina using OCT imaging for early diagnosis of diabetic retinopathy.** The microscopic size of nanotubes allows for ease of injection into the retina and into the retinal capillaries, while the outer coating of gold particles serves as a contrast agent in OCT imaging, allowing for higher resolution images due to enhanced signal.

BACKGROUND

Elevated glucose levels that result from diabetes cause damage to blood vessels which can lead to diabetic retinopathy [2]. One protein that plays a crucial role in the growth of new blood vessels during diabetic retinopathy is vascular endothelial growth factor (VEGF) which is activated when bound to its receptor, VEGFR2 [1]. Optical coherence tomography (OCT) is an imaging technique that uses light waves to capture 2D and 3D images images of the retina (Figure 1) [4].

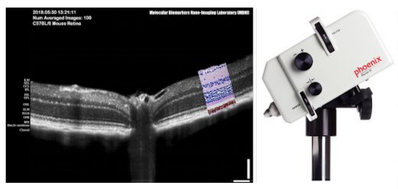

Figure 1. OCT image of mouse retina and OCT device.

OCT imaging is often used on patients with diabetic retinopathy to detect anatomical changes that occur as a result of the disease. In order to optimize OCT imaging, gold coated nanotubes will be used because the high electron density of gold enhances the contrast of the image due to a phenomenon called localized surface plasmon resonance [3].

Gold coated nanotubes can also be coated with targeting agents such as anti-VEGF that can bind to the VEGF present in the retina of patients with diabetic retinopathy [5]. Thus, the presence of these modified nanotubes detected through OCT imaging can allow for the early molecular diagnosis of diabetic retinopathy.

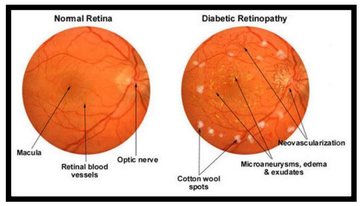

Figure 2. Angiography images of normal retina and retina of patient with diabetic retinopathy.

EXPERIMENTAL METHODS

1. **Synthesis of Silica Gel Solution:** Synthesize silica gel through sol-gel chemistry method using ethanol, triethylorthosilicate (TEOS), 1 M HCl solution (v/v 18:1:1) [6].
2. **Deposition of Silica Gel onto AAO Membrane:** Place bare Anodic Aluminum Oxide (AAO) membrane into silica gel solution. Sonicate for 5 minutes and remove surface gel layer from film. Leave films for overnight at 100° C.
3. **Template Dissolution:** Suspend films in 0.1 M NaOH solution for 2 hours to detach AAO membrane. Filter solution twice with water and once with ethanol to remove residue from the nanotubes' environment. Perform ultra sonication to achieve free silica nanotubes (SiNTs).
4. **Size Analysis:** Analyze SEM images of SiNTs and record height and diameter (top, middle, bottom) of to ensure adequate size distribution.

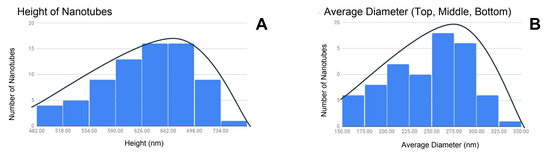

Figure 3. Size analysis of SiNTs; measurements recorded from SEM images.

5. **Fabrication of Gold Particles:** Suspend Au (20 mg/mL) in water. Add 1 mL Au-sol to 3 mL ethanol and 0.12 g/mL cysteamine to create gold particles coated with cysteamine. Suddenly add 0.1 mM sodium borohydrate to the solution and wait 3 hours.
6. **Coating of SiNTs:** Coat bare silica nanotubes in gold by mixing 18 mL EtOH, 1 mL silica nanotube solution, 1 mL gold particle solution. Wait 2 hours.
7. **Charge Analysis:** Measure zeta potential of bare SiNTs and gold-modified SiNTs to ensure that synthesis and modification were completed successfully.

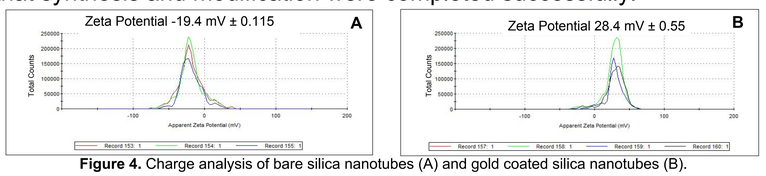

Figure 4. Charge analysis of bare silica nanotubes (A) and gold coated silica nanotubes (B).

RESULTS

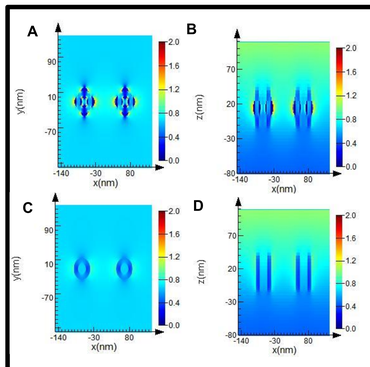

Figure 5. FDTD-simulated electrical field intensity on Au modified (A, B) and unmodified SiNTs (C, D).

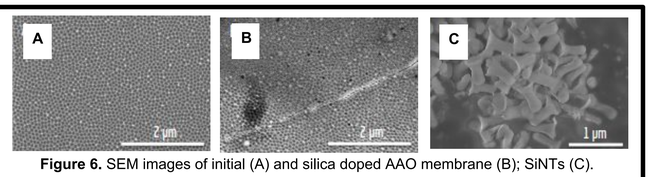

Figure 6. SEM images of initial (A) and silica doped AAO membrane (B); SiNTs (C).

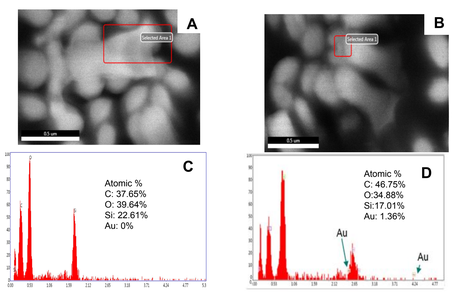

Figure 7. SEM image of Bare SiNT (A) and Gold Modified SiNT (B), EDX graph of Bare SiNT (C) and Gold Modified SiNT (D)

RESULTS - Continued

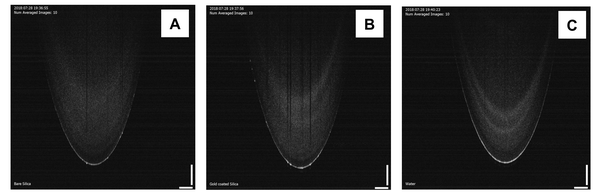

Figure 8. OCT images of water-based agar gel with bare SiNTs injected (A), and gold coated SiNTs injected (B) in the presence of blank control (C).

CONCLUSIONS AND FUTURE STEPS

SiNTs were produced by using sol-gel chemistry and template assisted strategy. The particles were coated with a thin gold layer and characterized via zeta potential measurement and EDX spectroscopy. SiNTs were included in water based agarose gels as a tissue equivalent phantom material. However, OCT images of gold coated silica nanotubes demonstrated a lack of enhanced signal in agar environment. The results indicate that the OCT images of the control group also emitted a signal, so the agar could be interfering with the signal of the SiNTs.

In the future, there are several possible developments:

- Enhance signal of gold coated silica nanotubes.
- Inject gold coated silica nanotubes into *in vitro* and *in vivo* retina.

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