NDnano Undergraduate Research Fellowship (NURF)
2015 Project Summary

1. Student name: Patricia Angelli Sosa Silva

2. Faculty mentor name: Dr. Ryan Roeder

3. Project title: Gadolinium nanoparticle contrast agent for MRI/CT dual mode imaging

4. New skills acquired:
During this project I learned to characterize nanoparticles by dynamic light scattering to measure the diameter of the nanoparticles. I learned to image phantom samples of different concentrations of gadolinium with micro-computed tomography and magnetic resonance, where different protocols were used to evaluate the T1 and T2 relaxation times, such as rapid imaging with refocused echoes.

5. Practical application use of your research:
Among the different imaging modalities, computed tomography (CT) and magnetic resonance imaging (MRI) are proficient diagnostic tools in the clinical field. Due to the limitations of each modality, combination of different imaging techniques may provide a more accurate and comprehensive diagnosis. In order further enhance CT and MRI, it would be necessary to develop contrast agents for multimodale imaging. Gadolinium has favorable characteristics which indicate it could be used in nanoparticles as a contras agent (CT: k-edge=50.2keV, MRI-T1 weighted: paramagnetic characteristics[1]).

Project summary:
Contrast agents in magnetic resonance affect the magnetization of hydrogen atoms in water molecules, which generate either a positive (T1) contrast or a negative (T2) contrast, depending on the characteristics of the material. Literature suggests that only the atoms in the surface of a nanoparticle interact with hydrogen atoms, hence the contrast is dependent on the by surface to bulk ratio, which is directly proportional to the diameter of the nanoparticle [2,3]. In order to evaluate this effect, rapid imaging with refocused echoes was realized to phantoms containing gadolinium concentrations between 0-2mM in order to obtain the longitudinal relaxation rate (Figure 1.a.). Since stability of the solution was an issue polyvinylpyrrolidone (PVP) was added in order to suspend the nanoparticles in water. In Figure 1.b. it is clear that the longitudinal relaxtivity (r1), the slope of the R1 and concentration graph, decreases as the diameter increases, with the exception of the 2-3nm diameter nanoparticles. However, the 2-3nm nanoparticle solution demonstrated to be unstable because the diameter measured in the DLS was of 290nm even after filtering it twice and doing various measures, so the instability of the 2-3nm nanoparticles could be the reason for this behavior.

a) b)

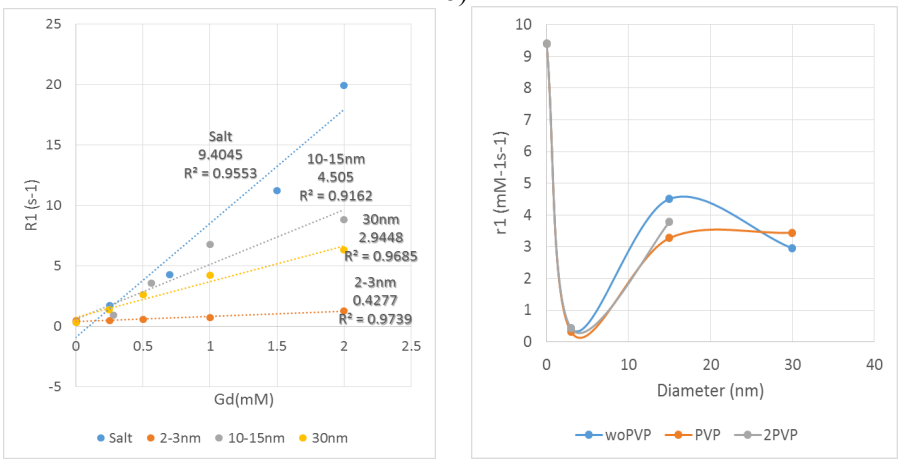

Figure 1. a) Longitudinal relaxation rate (R1) for different concentration of nanoparticles of various diameters. b) Change in longitudinal relaxivity (r1) due to diameter of nanoparticles.

In order to evaluate the viability of the nanoparticles as MRI/CT dual mode imaging contrast agents higher concentrations of gadolinium were used in the phantoms (0-10mM) for both CT and MRI. A gadolinium salt phantom was run first in order to ensure that the values would be above the detection limit for micro-CT, but the data for the different diameter nanoparticles showed a decreased attenuation and a variation between them (Figure 2.a.), which shouldn't happen considering that X-ray attenuation only depends on the concentration of the element[4]. This highlights the issue with the stability of the solutions, suggesting the nanoparticles may be falling out of solution and thus resulting in a decreased concentration. Longitudinal relaxivity lowered at higher concentrations due to the effect of the shortening of the T2 (Figure 2.b.).

a) b)

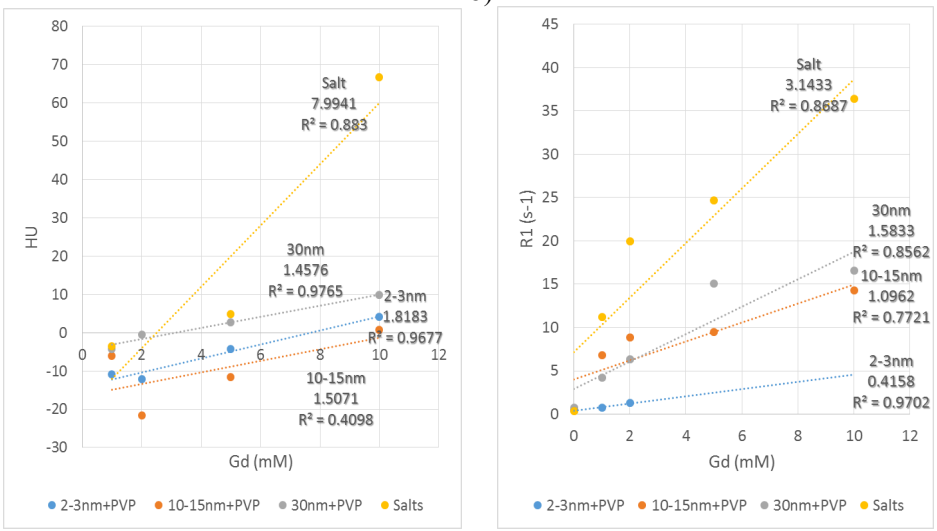

Figure 2. a) X-ray attenuation (HU) and b) longitudinal relaxation rate (R1) for different concentration of nanoparticles of various diameters.

Throughout the study it was possible to view how the change of diameter lowered the longitudinal relaxivity as it increased, but these are inconclusive due to the instability for the 2-3nm diameter nanoparticles. Also it was possible to view how increasing the concentration to enhance CT, since

attenuation is only dependent on the concentration, will affect a T1 weighted image due to the shortening of T2. This behavior will make gadolinium nanoparticles a challenging contrast agent if used for MRI/CT dual mode imaging because the changes of concentration to enhance CT could mean that MRI won't be able to generate a visible contrast.
To continue this investigation it is necessary to find a way to suspend the nanoparticles in a more efficient way in order to get conclusive results. Also finding a parameter for MRI that could overcome the issue of the T2 shortening would be of high importance and finally applying this to an animal model.

References:
[1] Paul, S. et. al. (2014) *Magnetic property study of Gd doped TiO2 Nanoparticles*. Journal of Alloys and Compounds: 601, 201-206
[2]Na, H.N. et. al. (2009) *Inorganic Nanoparticles for MRI Contrast Agent*s. Advanced materials: 21, 2133-2148
[3] Xu, W. et. al. (2014) *Paramagnetic nanoparticle T1 and T2 MRI contrast agents*. PCCP: 14, 12687-12700
[4] Cole, L. et. al. (2015) *Gold nanoparticles as contrast agents in x-ray imaging and computed tomopgraphy*. Nanomedicine: 10(2), 321–341