Cutting-off the oxygen and nutrient supply to a tumour leads to its death. Dr. Townley and her colleagues at Oxford University engineer deployable particles to do just that. This approach offers a different paradigm for anticancer treatment that eliminates the major disadvantage of systemic (and therefore non-selective) procedures. The goal is to minimize debilitating side-effects and sub-optimal outcomes of treatment by "starving" the tumour through its occluded vasculature (also known as embolization). But, what if these occlusion particles could also be traced via imaging?

The research group at University of Oxford developed polystyrene particles (PSPs) encapsulating tantalum oxide nanoparticles as an X-ray contrast agent to trace the fate of the microparticles in the tumor over time. This feature enhances the PSPs' primary role as physical occluding agents. The occlusion efficiency is measured by tracing the location and density of the PSPs over time. The imaging capacity is critical in non-invasive as well as invasive treatment procedures. For non-invasive procedures, the fate of the tumor can be visualized by MRI, thus, guiding the next stage of treatment and providing surveillance over time. In the case of invasive procedures, the fluorescent properties of the multimodal PSPs may indicate the tumor perimeter, delineating the tumour margins at the time of excision. In addition, sometimes the process of vasculature occlusion results in a “starved tissue” which can lose integrity and be excised through simple suction. The article is available [here](#).

One intriguing feature captured by this work relates to the use of tantalum oxide. Therefore, I asked Dr. Townley and her colleagues to elaborate further on the rationale for the selection of the contrast agent. The researchers opted to use a metallic element due to its stability. Neither the encapsulated tantalum-oxide, nor the PSPs, would be expected to degrade either as a consequence of time or as a result of the irradiation. In fact, the ionized tantalum would be expected to recombine with free electrons, reforming neutral atoms and allowing for doses beyond any conceivable therapeutic levels (in excess of 100,000 Gy) before significant deterioration such as brittleness or ageing would occur in the polystyrene capsule. This means that no loss of signal would be expected *in vivo*.

Dr Townley further elaborates on the advantage of a more permanent tracer. She explains that other imaging techniques use radioisotopes that depend upon the half-life of the tracer, which is usually short-lived. One of the most commonly used tracers is $^{18}$F-FDG with a half life of 110 min, whereas other commonly used radionuclides such as $^{99m}$Technetium and $^{201}$Thallium have half-lives of 6 hours and 72 hours, respectively. Yet, there is a clear need to evaluate the stage of tumor necrosis and tumor margins beyond a maximum timeline of 3 days afforded by these alternative tracers. It has been determined that approximately 7-9 days are required to achieve tumor necrosis after embolization. Therefore, the use of a permanent tracer, such as tantalum oxide, is advantageous.

The work of Dr. Townley and colleagues focuses on the particle synthesis, materials characterization, ex vivo testing, and modelling. This is just the beginning, setting the stage for additional evaluations in pre-clinical tumour mouse models. This will show where the nanoparticles accumulate in the tumour vasculature, verify that imaging can be performed at depth in the body of the mouse, and clarify whether there is any off-target toxicity by these particles. Occlusion of vessels by embolization particles is also often augmented by thrombus formation, which consequences can be investigated only *in vivo*.

A concern that always remains in translating results from pre-clinical models to humans is the actual relevance of the outcomes. Specifically, the extent of the findings that continue to be relevant, whileacknowledging the impact of pre-clinical study limitations. Dr. Townley cites Norbert Wiener who said "the best model for a cat is another cat, or preferably the same cat". She continues to elaborate that "in mice researchers often use xenograft models – these are easier to grow controllably and use human tissue. However, orthotopic models which are less predictable may be more realistic. Furthermore, mice may not be the best model for embolization [e.g. a rabbit system may be more similar]", an issue that the group is currently investigating.

So, how close is this technology to being applied in the clinic? Well, the first generation radiosensitizing embolization particles are currently awaiting commercialization for the purpose of augmenting traditional radiotherapy. As the current research gains momentum, and preliminary radiotherapy augmentation shows promise, its role in radiotherapy care is expected to develop and expand.
I would like to thank Dr. Townley and her colleagues for kindly agreeing to offer her research group’s vision on the future of targeted cancer therapy beyond the confines of the published scientific work.

To our readers: I am looking forward to your comments that can be sent to gabriela.voskerician@case.edu using the heading “Editors’ Choice”. We hope to develop this feature into a dynamic forum think-tank.