Shells on 90Yttrium Microspheres to Improve Radiopacity and Imaging Detection

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Background

Microspheres (MS), are an FDA-approved radioembolic device used to deliver selective internal radiation therapy (SIRT) for the treatment of primary and secondary hepatic malignancies (1). Access to the hepatic arterial system is commonly gained though the femoral artery, where a catheter is advanced to the relevant hepatic arterial branch supplying the target tumor or tumors (2). From there, millions of MS are infused into the downstream microvasculature to deliver targeted brachytherapy. Currently available intra- and post-operative imaging modalities have significant limitations with respect to confirming adequate MS distribution or identifying untreated areas (3). Consequently, further treatment decisions often must be delayed up to 3 months post SIRT until follow up cross sectional imaging is able to assess the impact of the treatment. To address this MS localization problem, a stable biocompatible chitosan shell imbedded with contrast agent (Iodine vs Bismuth) was applied to MS. With the successful envelopment of MS with contrast agent, intra- and post-operative cone beam CT imaging can potentially localize MS and areas of treatment or lack thereof. If successful in better evaluating MS distribution in the intra-op or immediate post-op period, this novel assessment technique will likely improve both the efficiency and effectiveness of SIRT for the treatment of hepatic malignancy.

Methods

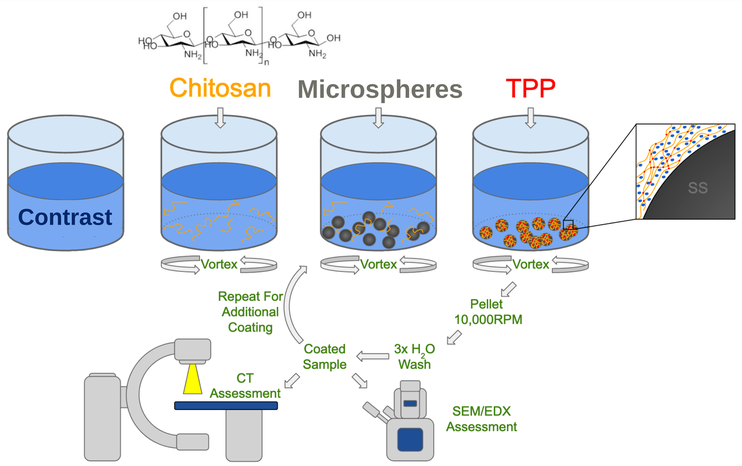

Figure 1: The above schematic depicts an overview of MS envelopment with chitosan and contrast (Iodine vs Bismuth). While under vortex conditions, 3mg/ml chitosan (along with 2.0% acetic acid) is dissolved in contrast solution. Radioactively decayed MS (bare or with previous coatings) are added to chitosan/contrast solution. Rapid crosslinking of chitosan ensues upon the addition of sodium triphosphate (TPP), where a chitosan shell with entrapped molecules of iodine/bismuth forms around the MS. The sample is put through centrifugation wash cycles (with H2O) to remove excess coating solutions. Samples can then be assessed with cone beam CT (figure 2), Scanning Electron Microscopy (SEM) (figure 3), and Elemental Dispersive X-Ray Spectroscopy (EDX) (figure 4).

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Results

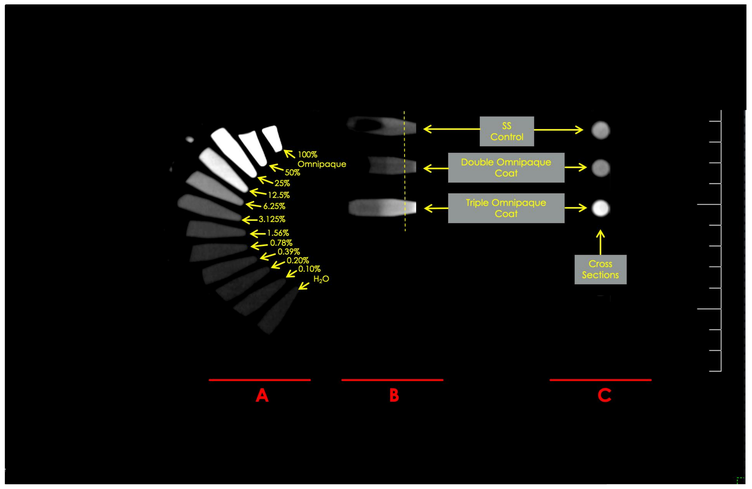

Figure 2: The above image features a combination of cross-sectional views taken with cone beam CT. (A) shows a control Iodine dilution profile. (B) shows imaging of MS without a chitosan shell (control), MS with a double chitosan/Iodine coat, and MS with a triple chitosan/Iodine coat. (C) shows a transverse cross-sectional view of each sample.

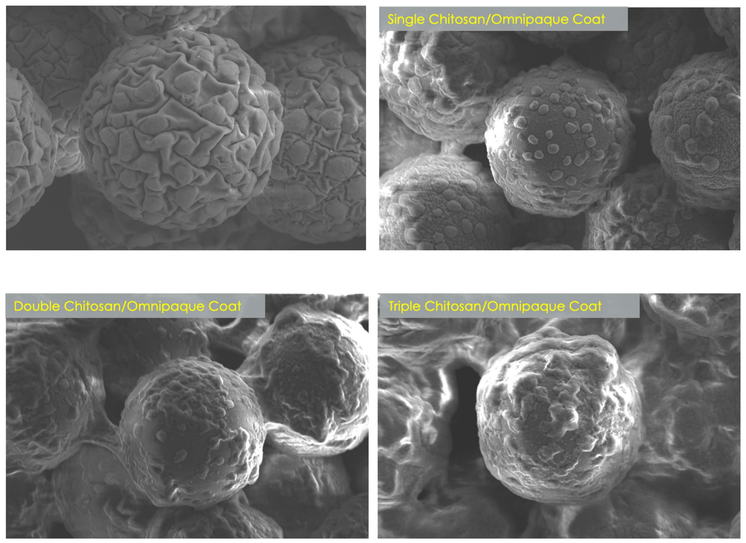

Figure 3: SEM images of (A) a MS without a chitosan shell, (B) MS with a single chitosan/Iodine coat, (C) MS with a double chitosan/Iodine coat, and (D) a MS with a triple chitosan/Iodine coat.

Results Continued

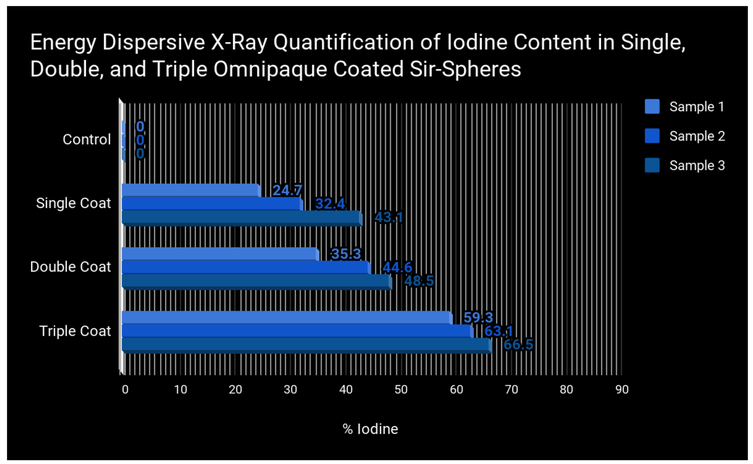

Figure 4: Elemental analysis results (specifically for Iodine) from EDX. Four conditions were measured with EDX: a control group which featured MS without a coating, MS with a single chitosan/Iodine coat, MS with a double chitosan/Iodine coat, and MS with a triple chitosan/Iodine coat. EDX was applied three times to each condition, measuring total iodine content of a single MS for each respective condition.

Conclusion

Currently, there is no standard protocol for post-SIRT imaging. In order to track post-operative tumor response, clinicians primarily rely on changes in tumor morphology and vascularity which may take up to 3 months to fully develop. This significant delay in tumor response assessment is a potential obstacle to patients receiving an appropriate and timely treatment regimen (2). The ability to intra-operatively assess SIRT dosage delivery would allow localization of treated and untreated regions. With this knowledge, other interventions can be applied to ensure a more efficacious treatment plan.

In this study we were able to apply significant amounts of radiopaque iodine to the surface of MS. With the utilization of SEM, EDX, and cone beam CT, we confirmed that we (1) successfully enveloped MS in crosslinked chitosan, (2) successfully entrapped iodinated molecules within this chitosan shell, and (3) successfully demonstrated visibility with cone beam CT of MS with the contrast shell.

References

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Images taken and prepared by study team

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