blocked (embolized) to cut off the blood supply of the tumor. Prior to embolization, a chemotherapeutic agent is injected into the artery to deliver it preferentially to the tumor cells. This approach leaves the hepatic portal vein intact and is therefore thought to preserve the health of non-tumor liver cells that mainly depend on it for blood supply. Recently, the use of beads that release chemotherapeutic agents over time have been suggested to increase the effectiveness of these treatments.

[0006] Similarly, transarterial radioembolization uses the same types of particles to block the blood supply of the tumor; however, instead of chemotherapeutic agents, the particles rely on radiation given off by isotopes such as Yttrium-90 (Y-90) embedded in the particles (microspheres) that are delivered to the tumor. A variant on this procedure, known as percutaneous local ablation, follows the radioembolization with multiple days of direct injections of ethanol to the tumor.

[0007] Lastly, there is microwave ablation that uses electromagnetic waves with frequencies greater than 900 kHz to heat the tumor to a temperature higher than 100 °C. This allows for a faster and more uniform ablation of the tumor, but studies have yet to show any statistical difference in efficiency compared to radioembolization.

[0008] The standard of care for patients with HCC considered too advanced for resection or localized ablation is systemic chemotherapy. The only treatment that has shown an improvement in mean survival of treatment groups is Bayer's Nexavar (sorafenib), which only prolongs survival by three months. Thus, there is a need for additional treatment options for HCC and other cancers.

SUMMARY

[0008a] In one aspect, provided herein is a method for producing liposome containing alginate microspheres comprising: Atomizing, ~~using an atomizer,~~ a liposome/alginate solution using an ultrasonic atomizer into a curing solution comprising an alginate cross-linker, and isolating liposome containing alginate microsphere having an average diameter of 20 to 80 μm.

[0008b] In another aspect, provided herein is a liposome containing alginate microsphere produced by the method as described herein comprising:

(a) an alginate microsphere having an average diameter of 20 to 80 μm; and

(b) liposomes dispersed in the alginate microsphere, the liposome containing a therapeutic and/or imaging agent.

[0008c] In another aspect, provided herein is the use of the liposome containing alginate microsphere as described herein in the manufacture of a medicament for treating cancer using embolization therapy, wherein the medicament is to be injected into the tumor vasculature of a subject.

[0008d] In another aspect, provided herein is a liposome containing alginate microsphere produced by the method as described herein~~thermotherapeutic alginate microsphere~~ comprising a thermotherapeutic agent encapsulated in an alginate microsphere.

[0008e] In yet another aspect, provided herein is the liposome containing alginate microsphere described herein for use in therapy.

[0009] Certain examples are directed to compositions comprising and method for producing liposome containing alginate microspheres, optionally the liposomes encapsulate a variety of useful substances. Substances of note that can be encapsulated in liposomes and loaded into alginate microspheres include radiotherapeutics (*e.g.*, rhenium-188), radiolabels (*e.g.*, technetium-99m), chemotherapeutics (doxorubicin), magnetic particles (*e.g.*, 10 μm iron nanoparticles), and radio-opaque material (*e.g.*, iodine contrast). In certain examples, rhenium-188 liposomes in alginate microspheres (Rhe-LAMs) can be used for treatment of liver tumors, specifically hepatocellular carcinoma (HCC). In a more particular example HCC treatment can be through radioembolization, where the microspheres block the blood supply

CLAIMS

1. A method for producing liposome containing alginate microspheres comprising: Atomizing, ~~using an atomizer,~~ a liposome/alginate solution using an ultrasonic nozzle into a curing solution comprising an alginate cross-linker, and isolating liposome containing alginate microsphere having an average diameter of 20 to 80 µm.

~~2. The method of claim 1, wherein the atomizer is an ultrasonic nozzle.~~

~~3~~2. The method of claim ~~1~~2, wherein the ultrasonic nozzle is a 1 Hz to 100 kHz nozzle.

~~4~~3. The method of claim ~~1~~2, wherein the ultrasonic nozzle is a 25 kHz nozzle.

~~5~~4. The method of claim 1, wherein the ~~atomizer~~ ultrasonic nozzle is positioned 1 to 10 cm from the curing solution.

~~6~~5. The method of claim 1, wherein the curing solution comprises a cation.

~~7~~6. The method of claim ~~5~~6, wherein the cation is selected from calcium, strontium, barium, iron, silver, aluminum, magnesium, manganese, copper, and zinc.

~~8~~7. The method of claim 1, wherein the curing solution comprises $CaCl_2$.

~~9~~8. The method of claim 1, wherein the liposome/alginate solution comprises a liposome to alginate ratio of 1:1.

~~10~~9. The method of claim 1, wherein the liposomes comprise a therapeutic agent or an imaging agent.

~~11~~10. The method of claim ~~9~~10, wherein the therapeutic agent is a thermotherapeutic, a chemotherapeutic, or a radiotherapeutic agent.

~~12~~11. A liposome containing alginate microsphere produced by the method of claim 1 comprising:

(a) an alginate microsphere having an average diameter of 20 to 80 µm; and

(b) liposomes dispersed in the alginate microsphere, the liposome containing a therapeutic and/or imaging agent.

~~13~~12. Use of the liposome containing alginate microsphere of claim 1~~12~~ in the manufacture of a medicament for treating cancer using embolization therapy, wherein the medicament is to be injected into the tumor vasculature of a subject.

~~14~~13. ~~A thermotherapeutic alginate microsphere~~A liposome containing alginate microsphere produced by the method of claim 1 comprising a thermotherapeutic agent encapsulated in an alginate microsphere.

~~15~~14. The microsphere of claim 1~~3~~4, wherein the thermotherapeutic agent is encapsulated in a liposome that is contained in an alginate microsphere.

~~16~~15. The liposome containing alginate microsphere of claim 1~~12~~ for use in therapy.