LABORATORY INVESTIGATION

In Vitro Capture of Small Ferrous Particles with a Magnetic Filtration Device Designed for Intravascular Use with Intraarterial Chemotherapy: Proof-of-Concept Study

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ABSTRACT

Purpose: To establish that a magnetic device designed for intravascular use can bind small iron particles in physiologic flow models.

Materials and Methods: Uncoated iron oxide particles 50–100 nm and 1–5 μm in size were tested in a water flow chamber over a period of 10 minutes without a magnet (ie, control) and with large and small prototype magnets. These same particles and 1-μm carboxylic acid–coated iron oxide beads were likewise tested in a serum flow chamber model without a magnet (ie, control) and with the small prototype magnet.

Results: Particles were successfully captured from solution. Particle concentrations in solution decreased in all experiments ($P < .05$ vs matched control runs). At 10 minutes, concentrations were 98% (50–100-nm particles in water with a large magnet), 97% (50–100-nm particles in water with a small magnet), 99% (1–5-μm particles in water with a large magnet), 99% (1–5-μm particles in water with a small magnet), 95% (50–100-nm particles in serum with a small magnet), 92% (1–5-μm particles in serum with a small magnet), and 75% (1-μm coated beads in serum with a small magnet) lower compared with matched control runs.

Conclusions: This study demonstrates the concept of magnetic capture of small iron oxide particles in physiologic flow models by using a small wire-mounted magnetic filter designed for intravascular use.

ABBREVIATIONS

IAC = intraarterial chemotherapy, MTC-DOX = magnetic targeted carrier bound to doxorubicin

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Figure E1 is available online at *www.jvir.org*.

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Innovative ideas to potentially alter the manner in which intraarterial chemotherapy (IAC) is administered have included the use of drug-eluting beads, extracorporeal filtration, and, in recent preclinical studies, an ionic resin–based filter (1–6). An intravascular magnetic device could potentially be used to selectively remove a magnetic targeted carrier therapeutic agent without the need for extracorporeal filtration/perfusion or nonselective ionic binding mechanisms. In the present study, we explore the in vitro feasibility of such a concept, testing a magnetic device to remove iron oxide particles from solution.

Small magnetic iron oxide particles can be bound to therapeutic agents such as doxorubicin and used in IAC or transarterial chemoembolization as an oncologic treatment like standard agents while offering the distinct abilities to be manipulated by a magnetic field and tracked by magnetic resonance imaging (7–15). Previous studies that used a magnetic targeted carrier bound to doxorubicin (MTC-DOX) showed that an external magnet placed over the liver of the patient could influence MTC-DOX distribution in patients with hepatocellular carcinoma (14,16). MTC-DOX was estimated to release 25% of the bound drug into human plasma over a period of 3 hours, but numerous different types of magnetic iron oxide particles have been bound to doxorubicin, with different affinities, stabilities, sizes, and behaviors in various microenvironments depending on the characteristics of the particles (7,8,10,15,17,18). Other agents and classes of medications, including thrombolytic agents, have also been bound to iron oxide particles and could potentially also be used with the technology developed in this investigation (7,8,19–21).

The magnetic properties of MTC-DOX or similar agents could potentially be used to remove the agents from the circulation, thereby decreasing systemic concentrations and toxicity and allowing dose escalation to provide a better therapeutic effect. The purpose of this proof-of-concept study was to establish that a magnetic intravascular device could bind small iron oxide particles in in vitro flow models. The hypothesis was that a small magnetic device could be designed and constructed for intravascular use and could capture iron oxide particles in vitro.

MATERIALS AND METHODS

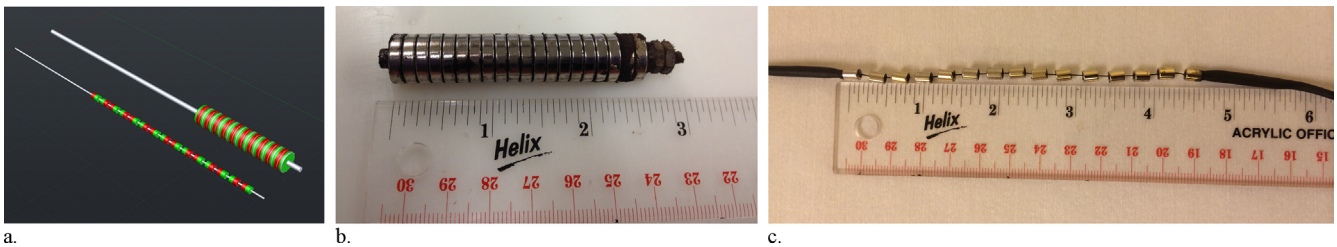
Magnetic Devices

An initial large prototype magnetic device was empirically constructed for initial in vitro experiments. This larger device consisted of 20 individual neodymium ring magnets (N52 grade, 12.5-mm outer diameter, 3-mm inner diameter, 3-mm length, estimated surface field of 3,400 G/0.34 T; K&J Magnetics, Pipersville, Pennsylvania) placed on a bolt in "cow magnet" configuration with like polarities facing and repelling each other and secured with a bolt (Fig 1). This larger device was used for initial flow chamber testing.

A second smaller device was constructed with size constraints to allow for eventual percutaneous introduction into the venous system (Fig 1). This device was constructed on a 0.014-inch-diameter guide wire (Transend 300 ES; Boston Scientific, Marlborough, Massachusetts) by using 15 neodymium ring magnets (N52 grade, 5-mm length, 4-mm outer diameter, 1-mm inner diameter, estimated surface field of 500 G/0.05 T; SuperMagnetMan Magnetics, Pelham, Alabama). These smaller magnets were placed on the 0.014-inch guide wire with like polarities facing and repelling each other. Approximately 3 mm of space was left between the repelling magnets to increase coverage and because the repelling magnetic forces could not be overcome easily. The proximal- and distal-end magnets were secured in position with layers of tape built up just beyond the magnet, heated shrink-wrap applied over the tape, and a small amount of glue adhesive. The overall length of the magnetic portion of this device was 11.5 cm. This device was introduced into an 18-F sheath with a one-way valve by using an introducer (Cook, Indianapolis, Indiana).

Particles

For initial testing, 50–100-nm uncoated iron oxide particles in powder form (iron[II,III] oxide; Sigma-Aldrich, St. Louis, Missouri) and 1–5-μm uncoated iron oxide particles in powder form (iron[II,III] oxide; Sigma-Aldrich) were selected. To evaluate more uniform coated particles in solution, iron oxide beads approximately 1 μm in size (800 nm by dynamic light scattering) with a COOH (carboxylic acid) coat in solution were selected



a. b. c.

Figure 1. Magnetic filtration devices. **(a)** Computer-aided design of the small and large magnetic filter devices demonstrates the alternating polarity design (ie, like poles facing and repelling each other). **(b)** The large magnetic filtration device and **(c)** the smaller wire-based magnetic filtration device.