Introduction Poly(vinyl alcohol) (PVA) is a biocompatible and biostable polymer that can be crosslinked to form nondegradable hydrogels that find applications in biomedicine [1]. Physically crosslinked PVA hydrogel produced using a low temperature thermal cycling (LTTC) process is noncytotoxic and possesses tunable mechanical and diffusion properties, which has been demonstrated to be extremely advantageous for many applications. In addition to physical crosslinking, iron oxide nanoparticles that are biocompatible and nontoxic have also been shown to provide a certain level of crosslinking in PVA [2]. In this work, we investigate the use of iron oxide as a crosslinking agent in conjugation with the low temperature thermal cycling (LTTC) process to form a degradable PVA hydrogel. This degradable PVA hydrogel could
find applications in many areas of biomedical engineering including as a scaffold for tissue engineering and as a controlled release/drug delivery vehicle. The introduction of iron oxide nanoparticles to a drug carrier system provides a means of magnetically targeting the therapeutic agent to the specific desired site. Furthermore, iron oxide has been studied significantly for use as a contrast agent, which allows for visualization of delivery [3]. The efficient production of uniform microbeads containing iron oxide for subsequent loading of drug molecules is a useful task to accomplish in this field. Following in vivo use of this biomaterial, clearance of the drug carrier or degradation of the scaffold is required, providing great need for this degradable PVA iron oxide hydrogel.

Materials and Methods

5% PVA dissolved in water at 90°C for 3 hours was used as the material matrix. Iron (II) and (III) chloride were dissolved into PVA and microbeads of 50-100 um were fabricated using microfluidic technology. A microchannel device was fabricated
from poly(methyl methacrylate) to achieve production of uniform beads by flowing the PVA iron salt solution, against an oil phase of hexane continuously, with a modified T-junction. Images of the uniform production of these microbeads were collected using a high-speed camera. Solidification of the beads was performed by precipitation of the iron through the introduction of an alkaline solution of NaOH. Beads turned to a dark colour and XRD confirmed the presence of iron oxide. Scanning electron microscopy (SEM) was completed to observe the nanoparticle distribution within the PVA matrix. Dissolution studies of PVA iron oxide material were performed on samples subjected to varying numbers of freeze-thaw cycles from 20°C to -20°C (at rate of 0.1°C/min) to achieve different degrees of physical crosslinking. PVA-iron microbeads were immersed in solutions containing ethylenediaminetetraacetic acid at concentrations of 0.1 to 1 M, as well as over a pH range of 2 to 10 using HCl and NaOH. Iron oxide dissolution is measured using atomic absorption spectroscopy, inductively coupled plasma atomic emission spectroscopy, and PVA dissolution will be measured gravimetrically. Additional work will include the PVA
iron oxide beads imaged under CT to display use as a contrast agent and injection into animal models will demonstrate its use practically.

Results

PVA iron oxide beads were produced through the microfluidic approach and analyzed by XRD to confirm the presence of Fe3O4. SEM images show the nanoparticle incorporation within the PVA matrix. Preliminary results of dissolution studies using AAS and gravimetric analysis demonstrate the release of iron and degradation of the material, as well as indication that an increase in PVA iron oxide material dissolution as pH is decreased. This illustrates the controlled dissolution of the biomaterial and details of the release kinetics will be reported. Results will show that varying the level of iron oxide crosslinking as well as physical crosslinking through LTTC will contribute to control over the rate of dissolution. CT images demonstrate the use of the microbeads as potential contrast agents for drug delivery.

Discussion and Conclusion
Results obtained display the dissolution of the PVA iron oxide biomaterial and the change in dissolution rates as a function of changes in processing parameters and environmental conditions. The ability to produce a degradable biocompatible hydrogel material is very beneficial for many biomedical applications. This material can be used as a delivery vehicle for therapeutic agents while allowing magnetic resonance imaging or computed tomography to visualize the location of delivery. Furthermore, the presence of iron oxide nanoparticles provides a means for magnetic targeting, allowing more efficient and less toxic drug delivery to a specific location. Alternatively, tissue engineering scaffolds comprised of this material could be useful due to the controlled dissolution properties as well as the potential for magnetic control over mechanical properties of scaffold fibres for promotion of cell adhesion and growth.

Fabrication of PVA iron microbeads using microfluidic device imaged using a high-speed
imaging system.

Scanning electron micrograph of PVA iron oxide microbead.
Scanning electron micrograph of PVA iron oxide microbead illustrating the presence of iron oxide nanoparticles.

References