

Lay Summary
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**Magnetic Resonance Imaging derived mural perfusion dynamics in Crohn's disease:
Pathophysiology and prediction of disease relapse.**

Crohn's disease is treated by medication to suppress the body's immune system and/or by surgery to remove the diseased bowel. The medications have side effects including predisposing to infection and possibly a higher risk of cancer and for this reason doctors keep the dose as low as they can and where possible withdraw medication completely.

Unfortunately in many patients the disease may return (relapse) when medication is withdrawn requiring further higher doses of treatment or repeat surgery. It is currently very difficult to predict which patients will relapse.

Microscopic examination of bowel affected by Crohn's demonstrates abnormal blood vessels supplying the bowel wall. It is believed that an abnormal reduction in blood supply may be one of the mechanisms causing the disease, or at least some of its manifestations, but the evidence is not clear cut. It is also suggested that if present, this abnormal blood supply may mean the patient is at higher risk of disease relapse, even if the bowel looks normal to the naked eye (for example on endoscopy).

Magnetic resonance imaging (MRI) is a safe non invasive test which images the bowel wall. Unlike barium tests and CT scanning, it does not use ionising radiation which is important given many patients with IBD are young and must undergo repeated imaging. Recent data from our group shows MRI can detect this abnormal blood supply in Crohn's disease. Specifically we inject into an arm vein a safe contrast medium (gadolinium), which is used in everyday clinical MRI anyway. We then measured how quickly and to what extent the bowel wall takes up the contrast. Measurements of contrast passage from the blood stream into the bowel wall allow us to infer information about the type and quality of blood vessels supplying the bowel. Our technique has been validated against histological analysis of the bowel wall vessels under the microscope.

This study will have 2 parts. The first part examines 15 Crohn's patients and 10 non-Crohn's patients undergoing planned bowel surgery. Detailed matching between MRI measurements of the bowel wall blood supply before the operation will be made to histological analysis of the vessels supplying the bit of bowel removed in order to gain more information as to the role of reduced blood supply in the cause or clinical manifestations of Crohn's. We will measure chemicals in the bowel wall which change when the blood supply is poor and correlate these with our MRI measurements. We will also produce resin casts of the vessels supplying the bowel wall in the restricted bits of bowel (so we can see the size and shape of the blood vessels) and carefully match them to the MRI scan images. This work will significantly build on our initial validation work and give further insights into the usefulness of measuring the blood supply to the bowel with MRI and whether it may have a role in the care of patients. For example new classes of drugs are being developed that target the blood supply to the bowel in Crohn's disease and MRI may be able to predict which patients will respond best and then monitor that response.

The second part will assess if MRI measurements of blood supply can themselves predict which patients will ultimately relapse after a reduction in current conventional medication. In particular, MRI will be performed in 15 patients after surgical removal of the diseased bowel and 20 patients undergoing withdrawal of long term medication. Patients will be followed for 6 months and we will analyse whether abnormal MRI blood supply measurements at the start can predict if patients will relapse with the next 6 months. MRI could therefore have a very important role in helping doctors decide in whom to withdraw medication and in whom to maintain/restart it.