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Should computed tomography be the modality of choice for imaging Crohn's disease in children? The radiation risk perspective

David J Brenner

Computed tomography (CT) and, more recently, CT enterography are excellent non-invasive tools for diagnosing Crohn's disease, and for subsequent assessment of the disease, before and after therapy.¹ In this light, and given the general availability and ease of use of CT machines, it is not surprising that CT is steadily replacing barium small-bowel follow-through as the radiological modality of choice for imaging Crohn's disease.

There is, however, a potential downside, which is the radiation exposure produced by the CT scan. By their nature, CT scans result in radiation doses which are very much at the high end of those produced in diagnostic radiology, simply because a CT scan is effectively a large number of individual images that are electronically combined to produce a three-dimensional image. The effective dose involved in a CT scan is not large, but it is typically two to six times larger than that from barium small-bowel follow-through. Because of the typical long-term remission/relapse pattern of Crohn's disease, together with the fact that is predominantly a disease of young people, Crohn's disease patients are often imaged multiple times which, of course, correspondingly multiplies the radiation dose.

In this light, the report by Desmond *et al*² in this issue of the journal (*see page 1524*) surveying trends in radiation exposure as a result of imaging Crohn's disease, is most welcome. The study, from Cork University Hospital, Ireland, together with a corresponding report from the US,³ paints a picture of increasing lifetime radiation exposures in Crohn's disease patients, due almost entirely to the increased use of CT. For example, the Irish study² estimated that the mean cumulative effective dose per Crohn's disease patient increased by about a factor of 3 in the past decade. Correspondingly, as reported in the US (Mayo Clinic) study,³ the balance between the numbers of small-bowel follow-throughs (SBFRs) and CTs performed to image Crohn's disease has moved from 90% vs 10% in 2003 in favour of SBFR, to 75% vs 25% in 2007 in favour of CT.

Should we be worried about the increased radiation exposure associated with the increased CT usage? After all, while the Irish study reports that mean cumulative radiation doses to Crohn's disease patients has increased 3-fold in the past decade (from 8 to 25 mSv), this is still not a large radiation dose. An estimate of the age-at-exposure averaged lifetime cancer mortality risk associated with a 25 mSv effective dose is about 1 in 1000, or 0.1%.^{4–6} One may, of course, ask whether such estimated radiation risks from CT are "real" or simply theoretical extrapolations from much higher-dose scenarios. In fact at

the average effective dose of 25 mSv^{2,3} (and certainly at 100 Sv or more, to which 10% of Crohn's disease patients were exposed²), there are direct epidemiological radiation-associated cancer-risk data^{7–9} from about 30 000 Japanese atomic-bomb survivors who were several miles away from the epicentres of the explosions at Hiroshima and Nagasaki, and who were exposed to just this same range of low doses as the Crohn's disease patients. This low-dose group in the two Japanese cities has been followed for more than 50 years, and shows a small but statistically significant increased cancer risk.^{7–9} Other large-scale epidemiological studies on populations exposed in this dose range have reached the same conclusion.¹⁰ Thus, in the context of the CT doses estimated in the Irish study (and the similar doses from the US study), we have direct epidemiological evidence of a small but significant increase in cancer risk due to the radiation exposure, without the need to extrapolate cancer risk estimates from higher doses, with all the attendant uncertainties that entails.

An important point that emerges from the Irish study² relates to children. In particular, patients who were diagnosed with Crohn's disease in childhood (under 17), were twice as likely as the 17–40-year-old age group to have a high cumulative radiation exposure (>75 mSv), despite the fact that the dose per single CT scan is typically lower in children than in adults.^{11,12} This issue of paediatric exposure is potentially important because of the increased sensitivity of children to radiation-induced cancer. For example a 10-year-old girl is, on average, about four times more sensitive to radiation-induced cancer than a 50-year-old woman.⁴ Coupling this with the observation that children with Crohn's disease are receiving higher cumulative radiation doses than adults with the disease,² it is clear that the use of CT for imaging Crohn's disease in children is of some concern. If the age-at-exposure averaged lifetime radiation-related cancer mortality risk were indeed typically 1 in 1000

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for Crohn's disease patients imaged with CT, the increased cumulative dose, together with the increased radiation sensitivity of a paediatric Crohn's disease patient, might increase this estimated mortality risk in children to as much as 1 in 300.

Given that almost 10% of all Crohn's disease patients are children,¹³ such high radiation-associated cancer risks must be of concern. What can be done for these children? Clearly there are alternatives to CT, probably the most promising being magnetic resonance imaging (MRI).¹⁴ Until recently, MRI imaging of Crohn's disease was highly suboptimal, hindered by motion artifacts and lack of appropriate contrast agents. However, in the past few years, the technology has markedly improved,^{14 15} particularly in the reduction of imaging time, down to only a few seconds. In a 2003 study of contrast-enhanced MRI of the terminal ileum in children with Crohn's disease, Laghi *et al*¹⁶ correlated their MRI findings with ileal endoscopy and histology, and found a high sensitivity (84%) and specificity (100%) for the detection of Crohn ileitis. Likewise in a subsequent study¹⁷ using contrast-enhanced MRI, sensitivity and specificity were both >90% for the detection of Crohn's disease in the paediatric small bowel.

Thus, while further studies are needed, it appears that contrast-enhanced MRI is, or will soon be, a viable option for imaging paediatric Crohn's disease. Given the

significant potential radiation risks associated with repeated paediatric CTs, MRI should perhaps be considered as a candidate to become the "first line" modality for imaging Crohn's disease in children. Of course there are also issues associated with MRI cost and availability to consider.^{14 15} But if we allow that CT remains the first-line modality for imaging adult Crohn's disease (ideally with reduced radiation doses from those currently delivered¹⁸), the necessary resources required to use MRI only for the <10% of Crohn's disease patients who are children, may become more feasible.

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Branch intraductal papillary mucinous neoplasms: just the tip of the iceberg?

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Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas have drawn considerable interest in recent years as we begin to learn more about the natural history of this disease. It is now commonly accepted that these tumours can be classified into two main categories according to their origin in the gland—that is main duct IPMN (MD-IPMN) and

branch duct IPMN (BD-IPMN). It is also well documented that IPMNs may progress through different stages of dysplasia into invasive carcinoma. It is, however, not well known whether all IPMNs ultimately progress into invasive cancer and if so what the timeline of this process is. In contrast to classical ductal adenocarcinomas of the pancreas, however, where patients always present with fully developed carcinoma with a dismal prognosis, many patients with IPMNs present early enough so that an intervention might prevent the development of pancreatic cancer. In fact, about 8–43% of

patients with MD-IPMNs and 54–94% of patients with BD-IPMNs present with non-malignant lesions.¹ Whereas it is well accepted that patients with MD-IPMN should undergo resection of the lesion at the time of diagnosis, current guidelines recommend non-surgical management of a certain subgroup of BD-IPMNs.¹ Asymptomatic patients with tumours <30 mm in size without mural nodules and without a main duct dilation (>6 mm) fall into this category. Of note, these recommendations were not based on long-term follow-up of such patients but on the extremely low incidence of invasive cancer of patients initially presenting with these features. Recently, follow-up studies regarding this issue have been published. Salvia *et al* followed 89 patients with low-risk BD-IPMNs over a median of 32 months; surgery was performed in only 5 of these patients due to an increase in size, and none of the surgical specimens demonstrated malignancy.² Tanno *et al* included 82 patients with low-risk BD-IPMNs in a similar

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