The new treatment paradigm for Barrett's dysplasia

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You are diagnosed with localised cancer. What are your options? A small cancer can be entirely removed with surgery. If it is larger, after debulking, the tumour field is ablated using radiotherapy.

So what happens if you have precancerous change such as mucosal dysplasia arising in Barrett's oesophagus? It should be easily curable. But sadly, until very recently, there was no local treatment. The doctor could offer regular endoscopic surveillance until cancer developed or perform oesophagectomy with its 30% morbidity rate and not insignificant mortality rate. Finally, the paradigm is changing.

The standard cancer treatment approach can be applied to Barrett's dysplasia. Debulking using endoscopic mucosal resection (EMR) followed by field ablation using radiofrequency ablation (RFA) has completely revolutionised treatment. Therapy is now performed as a day case and usually requires between two and three sessions spaced 2–3 months apart. There have been two randomised controlled trials (RCTs): one for both low-grade dysplasia (LGD) and high-grade dysplasia (HGD), and the second for LGD only. The first showed an 81% reversal of HGD and 91% reversal of LGD.¹ The second showed 92% success in LGD.² Although the studies have focused on RFA, EMR is always used first when lesions are seen.

In this edition of *Frontline Gastroenterology*, we have a report from one of the leading groups in the development of this new technology. Ortiz *et al*³ report their series of 50 patients who were treated for dysplasia at a single centre with EMR followed by RFA over the last 3 years (Ref, *Frontline Gastro* 2015). The focus of this paper is not on the clearance rate of dysplasia, but on the likelihood of detecting lesions which need to be debulked with EMR. These lesions can be very subtle, but the authors point out that in Wiesbaden,

arguably the most experienced European EMR centre, a visible lesion is detected in 80% of patients with intramucosal neoplasia. In the Nottingham experience published here, 76% of patients referred have already undergone EMR by the time of referral. Therefore, the numbers start out the same.

What the current paper shows, and what the experts know, is that more lesions tend to develop over time. The use of the word 'metachronous' in the title of this paper may be a little confusing as the authors define this as anything new detected from the moment of referral. Nonetheless, 40% of patients did develop new lesions, and some did so repeatedly.

Large national registries now exist, in the USA⁴ and ours, in the UK⁵ as well as a meta-analysis of more than 3800 patients from around the world.⁶ The Nottingham group have contributed to the 1200 patients collected from 25 UK centres as well as to the SURF LGD trial.² Rather to everyone's surprise, the registry data are at least as good as the results from the RCTs. Furthermore, our results are improving with time and clearance at 12 months for HGD is now 92%. Our registry has shown that this is almost certainly because our detection of very subtle lesions is improving and these are aggressively and comprehensively removed before starting RFA.⁷

For patients, two questions are crucial. First, am I being treated by the right doctor? The latest British Society of Gastroenterology guidance on Barrett's oesophagus makes it clear that ablative therapy must be undertaken in specialist centres.⁸ The current paper underlines how important this is. Further lesions appear, particularly if not completely removed at the initial EMR. These can be especially challenging to treat. Better endoscopic imaging leads to better detection and therefore better treatment. More expertise leads to better decision-making,

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and multidisciplinary team meetings are crucial to discuss the complex problems that arise in real life. Patients should undoubtedly be referred to centres of excellence as soon as a diagnosis of dysplasia is made, and preferably *before* the initial EMR is undertaken. The earlier and better dysplasia is treated, the better the long-term outcome is likely to be.

The second question is that of treatment durability. For oesophagectomy, the cure rate is almost 100%. For RFA, we now have 5-year follow-up data, suggesting durability rates in excess of 90% for those who are successfully treated. Data are also emerging that if new lesions develop they are also treatable with the same modality. We will not be certain until 10-year data become available as the natural history of HGD is that only 40% of patients develop cancer within 5 years.^{9 10} Oesophagectomy is, however, rapidly being replaced around the world by EMR and RFA as patients and physicians alike realise that there is a viable alternative to cracking a nut with a sledgehammer.

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Correction notice This article has been corrected since it was published Online First. The provenance and peer review statement has been corrected.

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