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Do patients have a choice?

Most cancer treatment options are reviewed at the weekly hospital multidisciplinary team (MDT) meetings where surgeons, oncologists, pathologists, radiologists, clinical nurse specialists and palliative care physicians meet to discuss patients' cases. A recommendation for the treatment plan is discussed and then offered to the patient when the clinician in charge meets them after the MDT meeting. In most cases, the patient will accept the recommendation made and the treatment is offered (1). However, if the patient refuses the recommended treatment, do patients have a choice? NICE guidelines clearly state that patients can refuse treatment to the extent of no treatment (1) but are they allowed an alternative treatment option without demanding it?

With the introduction of colorectal screening programmes the number of cases diagnosed with early rectal cancer is likely to increase. We should not treat all rectal cancers in the same way and we should personalise their treatments. Extirpative surgery should be avoided in early stage rectal cancer especially if it involves a permanent stoma in an older comorbid patient who is at high surgical risk or deemed not suitable for surgery.

The management of early rectal cancer has evolved slowly over the past decade and internationally there is a move to treat most early rectal cancer conservatively with alternative local treatment options. This includes either trans-anal endoscopic micro-surgery (TEMs) or contact x-ray brachytherapy (Papillon). General anaesthesia is necessary for TEMs (2). In patients who are not suitable for surgery or fit for anaesthesia, contact x-ray brachytherapy (Papillon) is an alternative option (3, 4, and 5). Contact x-ray brachytherapy (Papillon) is not new. It has been used in rectal cancer for over 80 years. Prof Jean Papillon from Lyon popularised this technique which bears his name. Papillon treated 312 patients and achieved local control in 91% of cases (3). His protégé Jean Pierre Gerard continued championing contact x-ray brachytherapy (Papillon) in Lyon and later moved to Nice. He had published many scientific papers including a randomised trial Lyon 96-02 (6). Sischy visited Lyon in the early seventies and started CXB facilities in the USA. He was able to replicate both Papillon's and Gerard's results with local control of 95% in his cohort of 227 patients (7). A British group from Clatterbridge visited Lyon in 1992 and started the first CXB facility at Clatterbridge Cancer Centre in 1993 (8). The first prototype machine made by a British company 'Ariane' was made available for clinical use at Clatterbridge in 2009. Over 1000 patients have now been treated at Clatterbridge using the new machine which is the world's largest cohort of patients treated by CXB. They are organising an international meeting on 24th March to celebrate their 25th anniversary of initiating CXB facilities in the UK this year. There are now 4 centres offering CXB in the UK and 12 centres around Europe. International Contact Radiotherapy Network group (ICONE) has been set up to coordinate its activities and research initiatives (9).

Contact x-ray brachytherapy (Papillon) is not suitable for all patients with rectal cancer. Careful case selection is important to get the best results. Only early small rectal cancers are suitable for radial treatment with the aim to cure and the following criteria serves as a guideline.

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Case selection for radical Papillon treatment

1. Histologically confirmed rectal cancer.
2. Well to moderately differentiated adenocarcinomas.
3. Size less than 3 cm in greatest diameter.
4. Stage T1, T2 (early tumours confined to bowel wall).
5. No suspicious lymph nodes in the pelvis.
6. Mobile, exophytic tumour.
7. Patients considered not suitable for surgery.
8. Location not higher than 12 cm from anal verge.
9. Patient must agree for regular long term follow up.

Cases not suitable for CXB

1. Poorly differentiated adenocarcinomas
2. Presence of Lympho-vascular invasion
3. Deeply infiltrating ulcerative fixed tumours
4. Tumour involving more than half the circumference

Larger (>3cm) or more advanced tumours (T3a /T3b) with possible lymph node metastases should be treated initially with external beam radiotherapy (EBRT) or chemoradiotherapy (10). If there is no residual tumour seen on endoscopy, or felt on palpation and if restaging MRI scan showed no evidence of residual tumour, these patients are considered to achieve a complete clinical response (cCR). There is increasing evidence that these patients do well without surgery. This approach of 'watch and wait' was started by a surgical group in Brazil and is becoming more popular among the surgeons and patients as this avoids extirpative surgery and a stoma (11). If there is good response with significant reduction in size, there is increasing evidence that down staging also occurs in patients who had surgery (12). If no further treatment is given after EBCRT, regrowth occurs in approximately 30% of cases who had achieved an apparent complete clinical response (13). Additional treatment with CXB boost can reduce the local regrowth rates to less than 10% (14). Therefore, those patients who are not suitable surgery or refuse surgery as it involve a stoma, contact x-ray brachytherapy can be offered to improve local control in patients with minimal residual disease after EBRT. We should not wait for local regrowths to occur as the probability of response to CXB is much lower when this happen. OPERA is a multi-centre phase 3 randomised trial set up by the international contact radiotherapy network group (ICONE) to evaluate the role of CXB boost after EBCRT. The trial has started in France and recruited 32 patients so far. Hopefully, it will start later this year in the UK.

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Contact x-ray brachytherapy can be delivered as outpatient. No general anaesthesia is necessary and therefore suitable for high risk patients who are not fit for anaesthesia. It can be treated in knee chest position or in lithotomy position. The treatment just takes just over a minute and the whole procedure can be carried out in about 20-30 minutes. Radiation applied dose of 30 Gy is given every 2 weeks which allows normal tissues to recover while the cancer cells are shaved off layer by layer at each treatment sessions. The treatment is targeted straight on to the tumour under direct visual control and very little normal tissues get irradiated. Therefore, unlike EBRT there is very little collateral damage to the surrounding normal tissues. As the low energy 50 KV x-rays has limited range of penetration and the dose at depth is confined to the first 10 mm with the radiation dose falling off rapidly at the depth beyond this. For tumour which respond well, there should be no visible or palpable tumour after two fractions and before the third fraction (15) [Figure 1]. Total dose of 90Gy is given in 3 fractions and final dose of 20 Gy can be given at the last fraction in patients who are not fit for surgery (total 110 Gy). The main side effect is bleeding which occurs in about 30% of cases which usually settle after about a year or two. Patients who are on anticoagulants may experience troublesome bleeding (G3) and argon plasma coagulation (ACP) can be offered to control the symptoms. About 10% of cases need this to control their bleeding. Superficial ulceration (radiation induced ulcer) can occur at the site of tumour in about 35% of cases. It is not painful and usually heals in about 3-6 months (16). There are no reported death associated with CXB treatment. The Royal College of Radiologists has included CXB in their recently published radiotherapy protocol, which has helped to clarify the indications for CXB (17).

Most national and international colorectal cancer guidelines recommend radical surgery for all stages of rectal cancer which is regarded as 'the standard of care' and it is likely that these recommendations will continue for the foreseeable future (1). However, there is no provision in these guidelines for older patients with multiple comorbidities who are not suitable for radical surgery. Most patients would like to avoid extirpative surgery and stoma, if they had a choice. They will accept inferior oncological outcomes and realised that surgical salvage can be offered later for their local recurrences (13, 18). Should they be given a choice for their treatment?

NICE has reviewed this procedure and published their recommendation in September 2015 as Interventional Procedure Guidance IP 532 (16). They recommend CXB procedure for patients not suitable for surgery and stated that there is enough evidence for its safety and efficacy. However, in patients suitable but refuse surgery, NICE recommend audit and research in this group of patients and accept that although there is enough evidence for safety there is a need to evaluate its efficacy. Clinical guidelines used published evidence to underpin their recommendations (exclusively quantitative) and NICE guidelines are no exception. However, evidence based clinical practice should also take into account patients preferences. This is achieved by patient involvement in the process and by using primary qualitative research, which uses techniques such as interviews to explore how and why patients make the decisions they do (19) Non-surgical management of rectal cancer by 'watch and wait' approach is becoming more acceptable approach to both clinicians and patients as it avoid extirpative surgery with a possible stoma (11, 13). Patient needs radiotherapy initially so that watch and wait approach could be offered. However, there is no provision for offering radiotherapy to early stage rectal cancer in the current NICE guidelines and colorectal MDTs continue to recommend the surgical option as 'the standard of care' (1). In older and co morbid patients whose number are increasing due to ageing population, this may not be the right treatment for their early low rectal cancer. There is a need to look for the alternative local treatment's options.

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Contact x-ray brachytherapy (CXB) could be regarded as one such option as it avoids surgery and possible stoma for low rectal cancers (5). It is likely that there will be increase in demand for this type of treatment approach both from the clinicians who up to this time, do not regard CXB as an option for treatment and also from the patients who are not aware of this treatment option. NICE guidance clearly states that for “proper inform consenting of patients, the patients and their carers should be fully aware of all the treatment options that are available and that they should be allowed to share in their treatment decisions” (1). Should patients be given that choice?

National bowel cancer screening has been ongoing for the past 10 years for patients age between 60-75 years and with the introduction of flexible endoscope screening from 55 years of age in the UK, the number of cases diagnosed with early rectal cancer will increase (20). These are the cases suitable for contact X-ray brachytherapy (Papillon). Clearly, extirpative surgery for their early rectal cancer can be regarded as an over treatment. It remains to be seen whether the practice of MDT recommendations with their paternalistic attitude in making decisions for their patients will continue or will they change their approach in the future and allow patients to make a choice for their treatment?

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Legends

Fig 1 – Showing treatment response for contact x-ray brachytherapy

- 1(a) Pre-treatment –showing malignant polyp 1
- (b) After one fraction showing good response1
- (c) After two fractions of CXB –no residual cancer seen.

1(a) Pre-treatment –malignant Polyp cT2 cN0 cM0 25mm at 5cm from anal verge



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1(b) After one CXB fraction



1(c) post treatment –no residual tumour

