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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 cases. A recommendation for the treatment plan is discussed and then offered to the patient when the clinician in charge meets him or her after MDT. In the majority of cases, patients accept the recommendation of the treatment being suggested [1]. However, if the patient refuses, does he or she 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 requesting it?

With the introduction of colorectal screening programme, the number of cases diagnosed with early rectal cancer will increase. We should not treat all rectal cancers, as today we are moving toward personalised (customised) treatments. Extirpative surgery should be avoided in early stage rectal cancer, especially if it involves a permanent stoma in an older co-morbid patient who is at high surgical risk. In some cases, patients may be deemed unsuitable for surgery.

The management of early rectal cancer has evolved slowly over the past decade; internationally there is a move to treat most early rectal cancer conservatively with alternative local treatment options. These include either trans-anal endoscopic micro-surgery (TEMS) or contact x-ray brachytherapy (CXB; Papillon). General anesthesia is necessary for TEMS [2]. In patients deemed unsuitable for surgery or unfit for anesthesia, contact x-ray brachytherapy CXB is an option [3-5]. It is nothing new and has been used in rectal cancer for over 80 years, having been popularised by Prof Jean Papillon (Lyon). He treated 312 patients and achieved local control in 91% of cases [3]. His protégé, Jean Pierre Gerard, continued championing CXB in Lyon and Nice, publishing many scientific papers, including one on a randomised trial in Lyon 1996-2002 [6]. Sischy visited Lyon in the early seventies and started CXB facility in the USA. He could replicate both Papillon's and Gerard's results, with local control of 95% in his cohort of 227 patients [7]. A UK group from Clatterbridge visited Lyon in 1992 and started the first CXB facility at the Clatterbridge Cancer Centre in 1993 [8]. The first prototype machine made by a British company 'Ariane' became available for clinical use in 2009. Over 1000 patients have now been treated here, using the new machine on the largest cohort of patients in the world. An international meeting has been organised on 24th March to celebrate the 25th anniversary of the CXB facility. There are now four centres offering CXB in the UK and 12 centres around Europe. The International Contact Radiotherapy Network group (ICONE) has been set up to coordinate its activities and research initiatives [9].

CXB is not suitable for all patients with rectal cancer, making careful case selection important to get the best results. Only early small rectal cancers are suitable for radical treatment, with the following criteria serves as guidelines in the aim to cure this cancer:

Case selection for radical Papillon treatment

1. Histologically confirmed rectal cancer.
2. Well to moderately differentiated adenocarcinomas.
3. Size <3 cm at the 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 unsuitable for surgery.
8. Location not >12 cm from anal verge.
9. Patient agree to regular long-term follow-up.

Cases unsuitable 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 shows 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 have had surgery [12]. If no further treatment is given after EBCRT, regrowth occurs in ~30% of cases who had achieved an apparent cCR [13]. Additional treatment with a CXB boost can reduce the local regrowth rates to <10% [14]. Therefore, those patients who are unsuitable for surgery or refuse surgery as it involves a stoma, CXB 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 happens. OPERA is a multi-centre phase 3 randomised trial set up by the (ICONE) to assess the role of CXB boost after EBCRT. The trial has started in France and recruited 32 patients to date. Hopefully, it will start later this year in the UK.

CXB can be given as an out patient treatment. No general anesthesia is necessary and therefore it is suitable for high risk patients who are unfit to be given anesthetics. It can be treated in knee-chest or lithotomy position. The treatment takes just over one minute and the whole procedure can be carried out in 20-30 minutes. A dose of radiation of 30 Gy is given every two weeks, which allows normal tissues to recover whereas the cancer cells are shaved off layer by layer at each session. The treatment is targeted straight at the tumour under direct visual control, such that very little normal tissues get irradiated. Therefore, unlike EBRT, there is very little collateral damage to the surrounding normal tissues. The low energy 50 KV x-rays have a limited range of penetration and the dose at depth is confined to the first 10mm, intensity falling off rapidly beyond this level. For tumours that respond well, there should be no visible or palpable tumour after 2 fractions and before the 3rd fraction [15] (Figure 1). Total dose of 90Gy is given in three fractions and final dose of 20Gy can be given at the last fraction in patients who are unfit for surgery (total 110Gy). The main side effect is bleeding, which occurs in ~30% of cases and usually settles after 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, required in ~10% of cases. Superficial ulceration (radiation-induced ulcers) can occur at the site of tumour in ~35% of cases. It is not painful and usually heals in 3-6 months [16]. There have been no reported deaths 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].

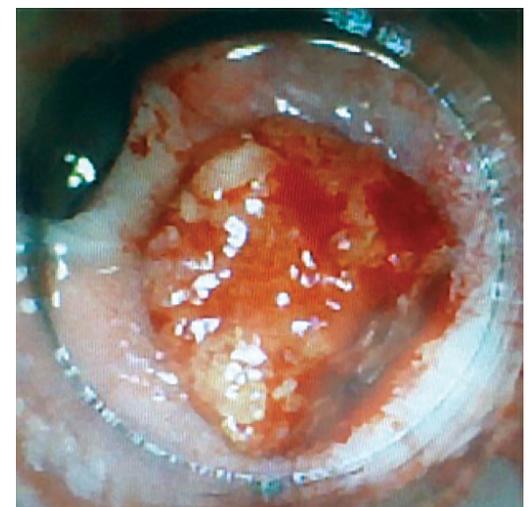
Most national and international colorectal cancer guidelines recommend radical surgery for all stages, which is regarded as 'the standard of care'; it is likely that this recommendation will continue for the foreseeable future [1]. However, there is no provision in these guidelines for older patients with multiple comorbidities making them unsuitable for radical surgery. Most patients given the choice would prefer to avoid extirpative surgery and stoma. They will

accept poorer oncological outcomes and realise that surgical salvage can be offered later for local recurrences [13,18]. Should they be given a choice for their treatment?

NICE has reviewed this procedure and published its recommendation in September 2015 as Interventional Procedure Guidance IP 532 [16]. They recommend CXB procedure for patients unsuitable for surgery, and stated that there is enough evidence for its safety and efficacy. However, in patients suitable for surgery but refuse it, NICE recommends audit and research in this group of patients and accept that, although there is sufficient evidence of safety, its efficacy needs to be assessed. Clinical guidelines have been based on published evidence to underpin their recommendations (exclusively quantitative) and NICE guidelines are no exception. However, evidence-based clinical practice should also take into account patient preferences. This is achieved by patient involvement in the process and by using primary qualitative research, including such techniques as interviews to explore how and why patients make their decisions [19]. Non-surgical management of rectal cancer by the 'watch and wait' approach is becoming more acceptable to both clinicians and patients as it avoid extirpative surgery with a possible stoma [11, 13]. Patient needs radiotherapy initially so that the watch and wait approach can 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 is 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 alternative local treatment options. 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 both from the clinicians who, up to this time, do not regard CXB as an option, and also from the patients who are unaware of this option. NICE guidance clearly states that for "proper inform consenting of patients, the patients and their carers



1 (a) Pretreatment – malignant Polyp. cT2 cN0 cM0 25mm at 5cm from anal verge.



1 (b) After one CXB fraction.



1 (c) post treatment – no residual tumour.

Figure 1 – Treatment response for contact x-ray brachytherapy
1 (a) Pretreatment - showing malignant polyp; 1 (b) After one fraction - showing good response;
1 (c) After 2 fractions - no residual cancer can be seen.

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 60–75 years old. 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 CXB. 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 about their treatment?

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