Review article

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# Understanding the anatomy of lymphatic drainage and the use of blue-dye mapping to determine the extent of lymphadenectomy in rectal cancer surgery: unresolved issues

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## Abstract

**Objective** This paper reviews the literature on the pathways of lymphatic drainage of the rectum and their significance in radical cancer surgery.

**Method** This paper reviews some of the seminal works on the lymphatic drainage of the rectum and its surgical implications when operating on patients with rectal cancer. Publications were searched via Medline, sourced from reference lists and by cross referencing with the most widely cited papers.

**Results** The classical European description of the anatomy of the lymphatic drainage of the rectum is presented. Early lymphatic mapping techniques and the role of newer technologies in lymphatic mapping, including sentinel lymph node mapping are discussed. The differing philosophies between Western practice, of dissection in the plane of the fascia propria and the Japanese wider pelvic lymphadenectomy are discussed.

**Conclusions** A clear understanding of the regional lymphatic drainage of the rectum and precise anatomical mobilisation of the rectum is the surgical cornerstone to excellent locoregional control of rectal cancer. The success of the differing Western and Japanese philosophies on the degree of pelvic lymphadenectomy suggests a possible role for 'selective wide pelvic lymphadectomy'. Mapping lateral lymphatic drainage pathways could augment the selection process for radiotherapy.

**Keywords** Anatomy of rectal lymphatics, lymphadenectomy, blue-dye mapping, rectal cancer

## Background

Rectal cancer is slow-growing and spreads in a mostly predictable and stepwise fashion through the layers of the rectal wall. This mode of direct spread is the basis of anatomical staging, as described by Cuthbert Dukes [1]. Rectal cancer spreads also via lymphatics, the blood stream and occasionally the peritoneal cavity when the tumour involves a *free* serosal surface [2].

Spread to regional lymph nodes is a critical event [1]. The usual route is via lymphatics to proximal nodes, although exceptions occur when these channels are obstructed by tumour. Intramural spread rarely extends beyond 2 cm from the visible edge of the tumour, except in advanced and high-grade tumours when distal intramural spread may occur. In 1942 Grinnell showed that lateral or downward intramural spread did not proceed without extensive involvement by tumour of proximal inferior mesenteric nodes [3]. This observation was later confirmed by Penfold [4].

Over the past two decades attention has been focused on the technique of precise anatomical dissection of the rectum, following Heald's widely-used concept of the 'Holy Plane' [5], which, in turn, is based on the original 1896 French description of the anatomy of the perirectal fascia and the retrorectal space provided by the Romanian surgeon-anatomist Tomas Jonnesco [6,7]. Also at that time, Gerota's injection studies illustrated in his article 'Die Lymphgefässe des Rectum und des Anus' clearly demonstrated that the lymphatics of the rectum were contained within this 'fascial envelope' [7,8]. These important anatomical observations together with the emphasis on mobilization of the rectum in the correct anatomical plane and preserving the perirectal fascia when operating for cancer

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are important predictors for both local recurrence (LR) [9,10] and survival [11–13].

There are however differing views about what constitutes an adequate lymphatic clearance necessary to achieve a potentially curative resection. For instance, in Japan some surgeons promote a wide lateral pelvic lymphatic clearance, although this practice is not frequently used in the West [14–17].

This paper reviews some of the seminal works on the lymphatic drainage of the rectum and its surgical implications when operating on patients with rectal cancer and discusses the use of blue-dye mapping. Publications were searched via Medline, using the following terms: *rectal cancer*, *rectal lymphatic anatomy*, *lymphatic mapping* and *pelvic lymphadenectomy*. Further publications were sourced from reference lists in appropriate publications and by cross referencing with the most widely cited papers. Only papers with a high impact factor addressing the subject matters were considered; although no publications were systematically excluded, this was not intended as an in-depth review and the anatomical studies and scope of the discussion is broad. The historical and foreign language publications were sourced locally and via the internet. Translations were provided by authors as required (PHC, JS).

## Classical European anatomical description of the lymphatic drainage of the rectum

The detailed understanding of the lymphatic drainage of the rectum is based on the lymphatic mapping techniques first developed in the late 1800s when Sappey introduced the use of mercury injection of cadavers [18]. However this technique had limited application to studying the rectum and it was Gerota who conceived the idea of using absolute black extractum alkanae, cinnabar or Prussian blue to better follow the lymphatic pathways [8,19]. He demonstrated that extractum alkanae, with its relatively weak colouring power, diffuses and stains the fat whilst cinnabar, ground in linseed oil and chloroform is only slightly penetrating. However, Prussian blue seemed to give the best results, particularly when mixed with spirit of turpentine and sulphuric ether and used immediately after mixing. Gerota's method was simpler and cheaper to use than Sappey's mercury injection technique, although the injected specimens were not as attractive. Furthermore, whereas the use of mercury had made histological examination impossible, blue-dye injections made it possible for use *in-vivo* without detracting from subsequent histological examination.

Gerota's work together with other studies of rectal lymphatics conducted by Quénu [20] and Marcille [21] promoted the concept of grouping the lymphatics of the rectum into three networks: intramural, intermediary and extramural which accompanied the arterial blood supply.

The details of the lymphatic networks were further studied and comprehensively described in 1925 when Villemin published his authoritative account of the lymphatic drainage of the anus and rectum, together with a resumé of work done by others in the field [22]. In his description, Villemin subdivided the rectum into upper and lower portions and promoted the concept that whereas the proximal rectum was topographically pelvic, its innervation and vascular supply were essentially related to the abdomen. He, and Jonnesco before him, considered the upper rectum as a terminal portion of the sigmoid colon (Jonnesco's so-called 'côlon pelvien') which had prolapsed into the pelvis [23]. It was clearly distinct from the lower rectum, which was topographically pelvi-perineal and terminated at the anus. Villemin described how the lymphatic trunks of the rectum accompanied the inferior, middle and superior rectal arteries and he referred to them as the inferior, middle and superior trunks. The former two collectively drained into perineo-pelvic-parietal nodes, clearly demonstrated by dissection of submucosal injection studies of the lower rectum. However, the superior trunk followed the superior rectal/inferior mesenteric arterial axis to drain into abdominal nodes as shown in injection studies of the upper rectum.

According to Villemin the inferior perineo-pelvic-parietal trunk took its origin from three to five channels, travelling through the subcutaneous tissues of the genito-crural aspect of the perineum and medial part of the buttock to drain into superficial inguinal nodes and then to external iliac nodes. Furthermore, he demonstrated that drainage was also possible to lateral pelvic nodes and to nodes close to the sacral promontory. Occasionally, drainage occurred to the internal iliac nodes. The middle trunk drained to nodes along the course of the internal, external and common iliac arteries and to nodes close to the sacral promontory. Villemin described the lymphatics of the lower rectum as draining to extra-pelvic (inguinal) and intra-pelvic (iliac and sacral) nodes, as well as to abdominal lymphatics along the course of the superior rectal artery. These lymphatics joined with those draining the posterior vagina and the levator ani. In Villemin's description, lymphatics of the upper (abdominal) rectum drained via the superior lymphatic trunk. This abdominal trunk consisted of short and long tributaries passing to rectosigmoid nodes and then followed the inferior mesenteric artery to the aorto-caval group of nodes. Occasionally, an accessory trunk could be seen to drain directly into the pre-caval nodes, bypassing those along the superior rectal and inferior mesenteric axes. Importantly, these lymphatics did not appear to communicate

  

with the lymphatics of other pelvic organs. In Villemin's description no distinction was made between anal and cutaneous tissue and the mucosa of the most distal rectum. He suggested that tumours of the lower rectum could and frequently did spread to inguinal nodes.

Miles' description of the lymphatic drainage of the rectum and his understanding of pelvic recurrence after perineal excision of the rectum was the basis for his operation of abdominoperineal excision. He first spoke of this in his Lettsomian Lecture to the Medical Society of London in 1923, subsequently published in The Lancet in 1925 [24] and again in 1926 [25]. His description of the lymphatic drainage was similar to that of Villemin, though Miles preferred to use the terms 'downward', 'lateral' and 'upward' zones of spread. This emphasized the importance of ischiorectal and inguinal, pelvic floor, internal iliac and the more common superior rectal-inferior mesenteric routes of lymphatic spread. Others also commented on these alternate pathways and Gilchrist pointed out the possibility of a squamous cell cancer of the anal canal spreading via superior rectal lymphatics and the need for an abdominoperineal excision of the rectum to treat this condition [26]. Further publications by Rouvière [27] and Coller [28] appeared documenting the widespread nature of lymphatic spread whilst others focussed on its distribution and the numbers of nodes involved [29,30]. It became apparent therefore that the wider and more extensive the resection, the greater the number of nodes likely to be identified and the greater the number found to be involved with tumour.

Coller's account of lymphatic metastases from rectal cancer reported a high prevalence of lateral zone metastases from low rectal cancers (36.8%), and emphasized 'the importance of wide excision of the tissues of the lateral zone of spread as well as the superior zone' for low rectal carcinomas and those of the anal canal [28]. It was noted also that the only lesions metastasizing to the lateral nodes were those arising in the most distal 3 cm of the rectum. In the early years of rectal cancer surgery, a major concern for surgeons was that of proximal nodes situated along the course of the superior rectal and inferior mesenteric vessels as they extended beyond the scope of the perineal resection as then practiced. As this operation was gradually replaced by the combined abdominoperineal approach the surgical emphasis shifted to a high ligation of the proximal arterial supply of the rectum so as to achieve a wider clearance of pelvic lymphatics.

In 1950 Blair, recognizing the trend towards sphincter preservation, set out to study in detail the lymphatic drainage of the anorectum in infant cadavers [31]. This work confirmed the general arrangement of inferior, middle and superior regions of lymphatic spread however, contrary to then popular beliefs he was unable to demonstrate lymphatic communications across the dentate line. In his study, the inferior efferent lymphatics from below the mucocutaneous junction were found to drain only to inguinal nodes whereas those above the mucocutaneous junction were limited to superior spread. This was confirmed when studying the low rectal efferents that drained laterally, but never inferiorly across the mucocutaneous junction, nor apparently, did these lymphatics perforate the levator ani muscles. Blair also made the important observation that the lateral drainage pathways were variable and inconsistent, especially when superior pathways were obstructed by cancer [31].

## A shift in direction – the Japanese experience

The early Japanese descriptions of rectal lymphatic drainage were similar to those published in the West. In 1927 Senba [29] published findings based on his detailed study of 200 foetuses. In 1940 Kuru [30] reported results of the clinical application of Senba's findings advocating a lateral lymph node dissection with high ligation of the inferior mesenteric artery. Although the lateral drainage pathways had been recognized by Western investigators, some Japanese surgeons now promoted the concept of a wide lateral pelvic dissection to incorporate this important, additional pathway [32–35]. They recognized the higher morbidity associated with such extensive lymphadenectomy [36,37] yet felt that this was clinically and socially acceptable because of their perception of this as a better cancer operation.

## Recent descriptions and concepts

With advances in nuclear medicine, there has been a renewed interest in the regional anatomy of the rectal lymphatics. Lymphoscintigraphy has been found to be accurate in mapping lymphatics in many parts of the body. It is commonly used in sentinel node biopsy of malignant melanoma and breast cancers [38,39] In breast cancer, it has been noted that sentinel node identification is superior when lymphoscintigraphy and blue-dye mapping are combined than with blue-dye alone, though accuracy and false-negative rates are similar [40].

Kaplan [41], Bucci [42] and Miscusi [43] pioneered the technique of rectal lymphoscintigraphy in the early 1980s using $^{99m}$Tc labelled colloid injected peritumourally. This new technology and subsequent work by Arnaud [44] demonstrated similar findings to that shown using dye injections. However, Arnaud highlighted the 'inconsistent and accessory pattern of lateral lymphatic drainage to internal iliac nodes' in 50% of control subjects

whose anal canal had been injected above the dentate line and stressed the importance of the site of tracer injection. He speculated that lateral spread may occur in rectal cancer when there is an obstruction of the cranial drainage pathway, as had Blair before him in his dissection studies [31]. Of course some of this could be due to the differences in the accompanying arterial supply, for example the wide variation in the reported presence of a middle rectal artery in the lateral ligament [45,46], so that one might question whether it is the *artery* that is variable or merely that it is a small vessel and hard to identify.

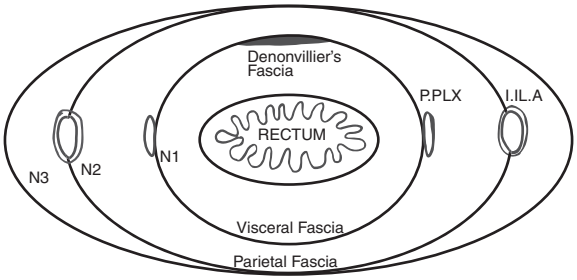


**Figure 1** Schematic representation of transection of mid-rectum, adapted from Takahashi et al.[53]. I.IL.A, Internal iliac artery; P.PLX, pelvic nerve plexus.

## Current surgical techniques

It is clear that precise dissection along anatomical planes is critical when mobilizing the rectum for cancer, involving, as it does, identification of the perirectal fascia and retrorectal space [7]. The aim in middle and low rectal cancers is to dissect the rectum and its perirectal fat enclosed by an intact perirectal fascial envelope. This approach has been variously described as total mesorectal excision (TME), [47], extra fascial dissection [48] and total anatomical dissection [10]. In upper-third tumours the same surgical principals apply but the perirectal fat may be transected 3–5 cm distal to the lower edge of the tumour. It is notable that lymphatic drainage passing laterally from the rectum along the lateral ligaments to lateral pelvic lymph nodes is outside the plane of dissection for *any* of these techniques. In the mid-1960s it was recognized that dissecting widely beyond the lateral ligaments risked injury to the pelvic autonomic nerves, with consequent urinary and sexual dysfunction [49]. Early studies by Woodburne [50] and later by Lee [51] gave a clear understanding of the anatomy of the pelvic autonomic nervous system. Enker acknowledged the close relationship of these nerves to the plane of dissection when he proposed a nerve-sparing wider pelvic resection [52].

## Japanese definitions of rectal dissection

Modern Japanese descriptions refer to three planes of dissection in the surgical approach to rectal cancer. The Western 'TME' is described as a 'limited resection'. A 'standard resection' involves dissection along the parietal pelvic fascia and the internal iliac artery whereas an 'extended resection' also includes excision of the internal iliac vessels preserving the superior vesical artery and obturator nerve, and is used by some Japanese surgeons (see Figs 1 and 2). This 'nerve sparing' operation involves the precise and detailed dissection of the pelvic autonomic nerves which are preserved whilst excising the surrounding lymphatic drainage pathways [53].

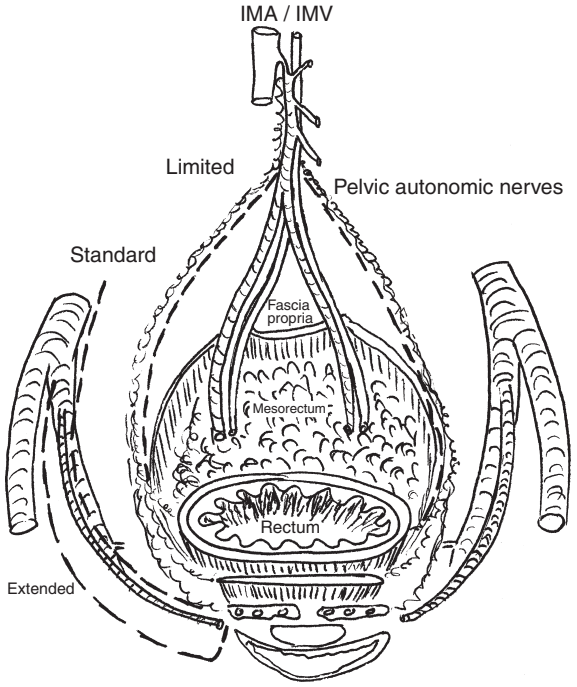


**Figure 2** Schematic representation of the three planes of dissection, adapted from Takahashi et al.[53].

## Controversies and unresolved issues

There is a considerable body of work from Japan arguing the case for wide pelvic lymphadenectomy as standard practice for low rectal cancer [35]. Whether an extended lymphadenectomy is justified for rectal cancer remains controversial. There are no prospective, randomized studies of its effect on LR and survival, although Enker has shown a statistically significant increase in five-year survival after extended lymphadenectomy in nonrandomized studies [52,54]. The main disadvantage of extended lymphadenectomy is an increase in the reported rates of sexual and urinary dysfunction. To avoid this, Japanese surgeons advocate lateral dissection with autonomic nerve-sparing, resulting in some improvement in the

rates of these complications. However, their oncological results do not differ from the results of MacFarlane [55] or Enker [56] performing TME *without* lateral lymphadenectomy. Other Japanese authors no longer routinely advocate a wide lateral pelvic dissection given the poor prognosis of patients with positive nodes [57]. It has also been reported that there is no difference in survival after surgery and neoadjuvant radiotherapy in patients whether or not they have undergone systematic lateral dissection [58]. Equally, Watanabe has shown that survival is equivalent whether patients undergo preoperative radiotherapy and/or lateral node dissection [59]. These issues were further debated by Yano and Moran, acknowledging the differences in Eastern and Western Practice [60].

## The sentinel node

There are two main advantages to sentinel lymph node detection as applied to other tumours. Firstly, the sentinel node has been shown to represent, and is used to evaluate, the draining lymph node basin without performing radical lymphadenectomy and secondly, detection can be improved with immunohistochemistry. Applying this to rectal cancer surgery is appealing although the clinical role of sentinel node mapping remains controversial as false negative rates are high and the sentinel node does not appear to accurately represent the lymph node basin [61].

One could postulate that the accurate mapping of the lymphatic drainage of an individual rectal cancer may provide the means to appropriately tailor the extent of surgery to a patient's particular circumstances. Given that the lateral lymphatic drainage of any rectal cancer is extremely variable and possibly unilateral, lymphatic mapping based on accurate anatomical localization of the predominant route of drainage beyond local, perirectal lymph nodes using a combination of pre-operative lymphoscintigraphy with intra-operative blue-dye mapping could assist in identifying those few patients who may benefit from a wide pelvic lymphadenectomy and adjuvant therapy. However, preliminary experience when using this approach, though eminently feasible, does not appear to improve the false-negative rate seen with intra-operative blue-dye mapping alone [62] and this dual approach remains experimental although useful in the detection of aberrant lymphatic drainage pathways; and possibly to investigate the prognostic significance of micrometastases and isolated tumour cells in lymph nodes.

## Summary

Undoubtedly, the emphasis on routine precise anatomical mobilization of the rectum has led to a substantial fall in LR rates. Some Japanese surgeons acknowledge the morbidity of a wide pelvic lymphadenectomy, but accept this and promote the approach in favour of the low rates of LR and perceived improved survival they achieve using this operation. The success of the two approaches to the surgical treatment of rectal cancer suggests a possible role for 'selective wide pelvic lymphadenectomy'. Also, if it could be shown that nodes outside the perirectal fascia contained metastatic tumour, this approach could form the basis for selecting patients for neoadjuvant or adjuvant radiotherapy.

In this way, a clear understanding of the regional lymphatic drainage of the rectum and its application to the treatment of rectal cancer using the techniques of lymphatic mapping may further improve and refine surgical outcomes.

## References


1 Dukes C. The classification of cancer of the rectum. *J Pathol Bacteriol* 1932; **35:** 323–32.
2 Keshava A, Chapuis PH, Chan C, Lin BPC, Bokey EL, Dent OF. The significance of involvement of a free serosal surface for recurrence and survival following resection of clinicopathological stage B and C rectal cancer. *Colorectal Dis* 2007; **9:** 609–18.
3 Grinnell RS. The lymphatic and venous spread of carcinoma of the rectum. *Ann Surg* 1942; **116:** 200–316.
4 Penfold JC. A comparison of restorative resection of carcinoma of the middle third of the rectum with abdominoperineal excision. *Aust N Z J Surg* 1974; **44:** 354–6.
5 Heald RJ. The holy plane of rectal surgery. *J R Soc Med* 1988; **81:** 503–8.
6 Jonnesco T 1901 Appareil digestif (Volume IV, 2nd edition). In: *Traité D'Anatomie Humaine.* (eds Poirier P, Charpy A), pp. 372–3. Masson et Cie, Paris.
7 Chapuis P, Bokey L, Fahrer L, Sinclair G, Bogduk N. Mobilisation of the rectum – anatomical concepts and the bookshelf revisited. *Dis Colon Rectum* 2002; **45:** 1–9.
8 Gerota D. Die Lymphgefässe des Rectums und des Anus. *Archiv für Anatomie und Physiologie Ann Abt* 1895: 240–56.
9 Quirke P, Durdey P, Dixon MF, Williams NS. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of internal tumour spread and surgical excision. *Lancet* 1986; **2:** 996–9.
10 Bokey EL, Öjerskog B, Chapuis PH, Dent OF, Newland RC, Sinclair G. Local recurrence after curative excision of the rectum for cancer without adjuvant therapy: role of total anatomical dissection. *Br J Surg* 1999; **86:** 1164–70.
11 Porter GA, Soskolne CL, Yakimets WW, Newman SC. Surgeon-related factors and outcomes in rectal cancer. *Ann Surg* 1998; **227:** 157–67.
12 McArdle CS, Hole D. Impact of variability among surgeons on postoperative morbidity and mortality and ultimate survival. *Br Med J* 1991; **302:** 1501–5.

13 Kessler H, Hermanek P. Outcomes in rectal cancer surgery are directly related to technical factors. *Semin Colon Rectal Surg* 1998; **9:** 247–53.
14 Koyama Y, Moriya Y, Hojo K. Effects of extended systematic lymphadenectomy for adenocarcinoma of the rectum – significant improvement of survival rate and decrease of local recurrence. *Jpn J Clin Oncol* 1984; **14:** 623–32.
15 Moriya Y, Hojo K, Sawada T, Koyama Y. Significance of lateral node dissection for advanced rectal carcinoma at or below the peritoneal reflection. *Dis Colon Rectum* 1989; **32:** 307–15.
16 Moreira LF, Hizuta A, Iwagaki H, Tanaka N, Orita K. Lateral lymph node dissection for rectal carcinoma below the peritoneal reflection. *Br J Surg* 1994; **81:** 293–6.
17 MacFarlane JK. (1997) Lateral node dissection – a critique. In: *Rectal Cancer Surgery. Optimisation Standardisation Documentation* (eds Søreide O, Norstein J), pp. 255–63. Springer-Verlag, Berlin.
18 Sappey C. (1885) *Description et Iconographie des Vaisseaux Lymphatiques Considérés Chez L'homme et les Vertébrés.* Delahaye, Paris.
19 Delamere G, Poirier P, Cunéo B (1913) *The Lymphatics* (Translated by Leaf CH). Constable & Co, London. p. 60.
20 Quénu E. Vaisseaux lymphatiques de l'Anus. *Bullet de la Société anatom de Paris* 1893; **5:** 399–409.
21 Marcille M (1902) *Lymphatiques et Ganglions Ileopelviens.* Thèse de Paris. Université de Paris, Paris.
22 Villemin F, Huard P, Montagné M. Recherches anatomiques sur les lymphatiques du rectum et de l'anus. Leurs applications dans le traitment chirurgical du cancer. *Rev de chir* 1925; **63:** 39–80.
23 Jonnesco T (1892) *Le Côlon Pelvien Pendant la vie Intra-Utérine.* Thèse. Lemale et Cie, Havre.
24 Miles WE. (1926) *Cancer of the rectum.* (Lettsomian lectures, 1923). Reprinted from *Transactions of the Medical Society of London* vol. xlvii, viii. Harrison & Sons, London.
25 Miles WE. The spread of cancer of the rectum. *Lancet* 1925; **205:** 1218–9.
26 Gilchrist RK, David VC. Lymphatic spread of carcinoma of the rectum. *Ann Surg* 1938; **108:** 621–37.
27 Rouvière H. (1932) *Anatomie des Lymphatiques de L'homme.* Masson et Cie, Paris.
28 Coller FA, Kay EB, MacIntyre RS. Regional lymphatic metastasis of carcinoma of the rectum. *Surgery* 1940; **8:** 294–311.
29 Senba Y. An anatomical study of lymphatic system of the rectum (in Japanese). *J Hukuoka Med Coll* 1927; **20:** 1213–68.
30 Kuru M. Cancer of the rectum (in Japanese). *J Jpn Surg Soc* 1940; **41:** 832–77.
31 Blair JB, Holyoke EA, Best RR. A note on the lymphatics of the middle and lower rectum and anus. *Anat Rec* 1950; **108:** 635–43.
32 Sugihara K, Moriya Y, Akasu T, Fujita S. Pelvic autonomic nerve preservation for patients with rectal carcinoma. Oncologic and functional outcome. *Cancer* 1996; **78:** 1871–80.
33 Moriya Y, Sugihara K, Akasu T, Fujita S. Importance of extended lymphadenectomy with lateral node dissection for advanced lower rectal cancer. *World J Surg* 1997; **21:** 728–32.
34 Mori T, Takahashi K, Yasuno M. Radical resection with autonomic nerve preservation and lymph node dissection techniques in lower rectal cancer surgery and its results: the impact of lateral lymph node dissection. *Langenbecks Arch Surg* 1998; **383:** 409–15.
35 Sugihara K, Kobayashi H, Kato T, Mori T, Mochizuki H, Kameoka S, Shirouzu K, Muto T. Indication and benefit of pelvic sidewall dissection for rectal cancer. *Dis Colon Rectum* 2006; **49:** 1663–72.
36 Scholefield JH, Steup WH. Surgery for rectal cancer in Japan. [letter]. *Lancet* 1992; **340:** 1101.
37 Harnsberger JR, Vernava VM III, Longo WE. Radical abdominopelvic lymphadenectomy: historic perspective and current role in the surgical management of rectal cancer. *Dis Colon Rectum* 1994; **37:** 73–87.
38 Thompson JF. The Sydney Melanoma Unit experience of sentinel lymphadenectomy for melanoma. *Ann Surg Oncol* 2001; **8:** 44–7.
39 Veronesi U, Paganelli G, Viale G *et al.* A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. *N Engl J Med* 2003; **349:** 546–53.
40 Hung WK, Chan CM, Ying M, Chong SF, Mak KL, Yip AWC. Randomised clinical trial comparing blue dye with combined dye and isotope for sentinel lymph node biopsy in breast cancer. *Br J Surg* 2005; **92:** 1494–7.
41 Kaplan WD. Iliopelvic lymphoscintigraphy. *Semin Nucl Med* 1983; **13:** 42–53.
42 Bucci L, Salfi R, Meraviglia F, Mazzeo F. Rectal lymphoscintigraphy. *Dis Colon Rectum* 1984; **27:** 370–5.
43 Miscusi G, Masoni L, Dell'Anna A, Montori A. Normal lymphatic drainage of the rectum and anal canal revealed by lymphoscintigraphy. *Coloproctology* 1987; **3:** 171–4.
44 Arnaud JP, Bergamaschi R, Schloegel M, Ollier JC, Haegele P, Grob JC, Adloff M. Progress in the assessment of lymphatic spread in rectal cancer. Rectal endoscopic lymphoscintigraphy. *Dis Colon Rectum* 1990; **33:** 398–401.
45 Ayoub S. Arterial supply to the human rectum. *Acta Anat* 1978; **100:** 317–27.
46 Sato K, Sato T. The vascular and neuronal composition of the lateral ligament of the rectum and rectosacral fascia. *Surg Radiol Anat* 1991; **13:** 17–22.
47 Heald RJ, Moran BJ, Rydall RD, Sexton R, MacFarlane JK. Rectal cancer – the Basingstoke experience of total mesorectal excision 1978–1997. *Arch Surg* 1998; **133:** 894–9.
48 Hill GL, Rafique M. Extrafascial excision of the rectum for rectal cancer. *Br J Surg* 1998; **85:** 809–12.
49 Bernstein WC, Bernstein EF. Sexual dysfunction following radical surgery for cancer of the rectum. *Dis Colon Rectum* 1966; **9:** 328–32.
50 Woodburne RT. The sacral parasympathetic innervation of the colon. *Anat Rec* 1956; **124:** 67–76.
51 Lee JF, Maurer VM, Block GE. Anatomic relations of pelvic autonomic nerves to pelvic operations. *Arch Surg* 1973; **107:** 324–8.

52 Enker WE, Laffer UT, Block GE. Enhanced survival of patients with colon and rectal cancer is based upon wide anatomic resection. *Ann Surg* 1979; **190:** 350–60.
53 Takahashi T, Ueno M, Azekura K, Ota H. (1997) The lymphatic spread of rectal cancer and the effect of dissection: Japanese contribution and experience. In: *Rectal Cancer Surgery. Optimisation Standardisation Documentation* (eds Søreide O, Norstein J), pp. 165–80. Springer-Verlag, Berlin.
54 Enker WE, Pilipshen SJ, Heilweil ML, Stearns MW Jr, Janov AJ, Hertz RE, Sternberg SS. *En bloc* pelvic lymphadenectomy and sphincter preservation in the management of rectal cancer. *Ann Surg* 1986; **203:** 426–33.
55 MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. *Lancet* 1993; **341:** 457–60.
56 Enker WE, Thaler HT, Cranor ML, Polyak T. Total mesorectal excision in the operative treatment of carcinoma of the rectum. *J Am Coll Surg* 1995; **181:** 335–46.
57 Ueno M, Oya M, Azekura K, Yamaguchi T, Muto T. Incidence and prognostic significance of lateral lymph node metastasis in patients with advanced low rectal cancer. *Br J Surg* 2005; **92:** 756–63.
58 Nagawa H, Muto T, Sunouchi K, Higuchi Y, Tsurita G, Watanabe T, Sawada T. Randomised controlled trial of lateral node dissection *versus* nerve preserving resection in patients with rectal cancer after preoperative radiotherapy. *Dis Colon Rectum* 2001; **44:** 1274–80.
59 Watanabe T, Tsurita G, Muto T, *et al.* Extended lymphadenectomy and preoperative radiotherapy for lower rectal cancers. *Surgery* 2002; **132:** 27–33.
60 Yano H, Moran BJ. The incidence of lateral pelvic side-wall nodal involvement in low rectal cancer may be similar in Japan and the West. *Br J Surg* 2008; **95:** 33–49.
61 Bell SW, Mourra N, Fléjou JF, Parc R, Tiret E. Ex-vivo sentinel lymph node mapping in colorectal cancer. *Dis Colon Rectum* 2004; **48:** 74–9.
62 Tiffet O, Kaczmarek D, Chambonnière ML, Guillan T, Baccot S *et al.* Combining radioisotopic and blue-dye technique does not improve the false-negative rate in sentinel lymph node mapping for colorectal cancer. *Dis Colon Rectum* 2007; **50:** 962–70.