

## Classification of radical hysterectomy

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Since the first publications about surgery for cervical cancer, many radical procedures that accord with different degrees of radicality have been described and done. Here, we propose a basis for a new and simple classification for cervical-cancer surgery, taking into account the curative effect of surgery and adverse effects, such as bladder dysfunction. The international anatomical nomenclature is used where it applies. For simplification, the classification is based only on lateral extent of resection. We describe four types of radical hysterectomy (A–D), adding when necessary a few subtypes that consider nerve preservation and paracervical lymphadenectomy. Lymph-node dissection is considered separately: four levels (1–4) are defined according to corresponding arterial anatomy and radicality of the procedure. The classification applies to fertility-sparing surgery, and can be adapted to open, vaginal, laparoscopic, or robotic surgery. In the future, internationally standardised description of techniques for communication, comparison, clinical research, and quality control will be a basic part of every surgical procedure.

### Introduction

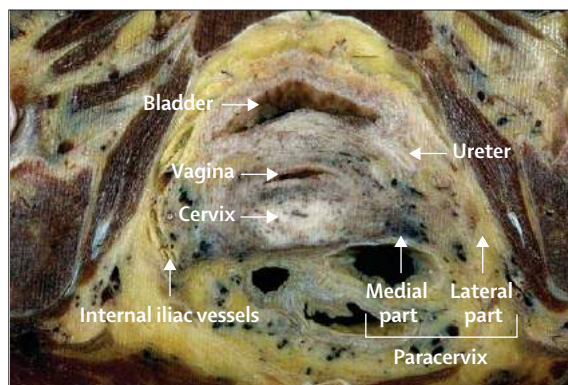
Tailoring has become a major issue in cancer surgery. Adaptation of radicality to tumour spread is an important topic in cervical cancer. On one hand, such adaptation has led to the development of ultraradical surgery; on the other hand, it has led to more-limited (ie, modified radical) surgery based on the idea of the surgical margin and on the estimated risk of pericervical spread, knowing that cervical cancer can spread in any direction.<sup>1</sup> Furthermore, the idea of wide excision has been validated in other tumours, including melanomas; sarcomas; and those of the aerodigestive tract, breast, and vulva.

As a result, the term “radical” or “extended” hysterectomy encompasses various types of surgery. Since the first publications of large series of surgeries for cervical cancer by Wertheim in Austria,<sup>2</sup> and later by Okabayashi in Japan<sup>3</sup> and Meigs in the USA,<sup>4</sup> many radical procedures that accord with different degrees of radicality have been described and done. These procedures give different names for the same anatomical structures and define these structures according to different interpretations of anatomy. The first publications in German or Japanese language are not consulted routinely. The wide use of eponyms adds confusion: original descriptions change over time with transmission by teaching, with writings that quote names but that do not refer to the original papers, and with the addition of minor surgical variants (some original, some redundant, and some ignoring previous descriptions of the same variants).

The rationale for a standardised international classification of radical hysterectomy includes: clarification of the details of common variations; standardisation of nomenclature in reports and publications, clinical protocols, and randomised controlled trials; assessment of complications and side-effects; and education and training. Investigators, trained gynaecological oncologists, and general gynaecologists—who may not be familiar with the anatomy of the retroperitoneal space—and fellows and residents in training should speak the same language.

The Piver–Rutledge–Smith classification published in 1974<sup>5</sup> has achieved substantial popularity, whereas the

1975 Symmonds classification was not adopted.<sup>6</sup> The former describes five classes of radical hysterectomy, but has several major drawbacks. It is misused by many researchers and surgeons because the tradition is transmitted orally without careful reading of the original paper.<sup>5</sup> The original paper does not refer to clear anatomical landmarks or international anatomical definitions. The vaginal extent of resection is systematically attached to pericervical extent; vaginal resection is excessive—from a third to three-quarters of the vagina. It includes a class I category, which is not radical hysterectomy, and a class V category, which is no longer used. The rationale and anatomy for differentiation between class III and IV are unclear. Surgeons frequently need to define intermediate classes between that of II and III (eg, II-III or II-and-a-half). The classification by Piver and colleagues<sup>5</sup> does not take into account the idea of nerve preservation that was introduced in the 1950s,<sup>7</sup> subsequently refined by Japanese surgeons,<sup>8–10</sup> and adopted by European surgeons.<sup>11,12</sup> Moreover, other types of ultraradical surgical procedures<sup>13–15</sup> and fertility-preserving surgery introduced by French surgeons<sup>16</sup> have been developed that are not included in the classification. Finally, the Piver–Rutledge–Smith classification applies only to open surgery, and does not take into account the

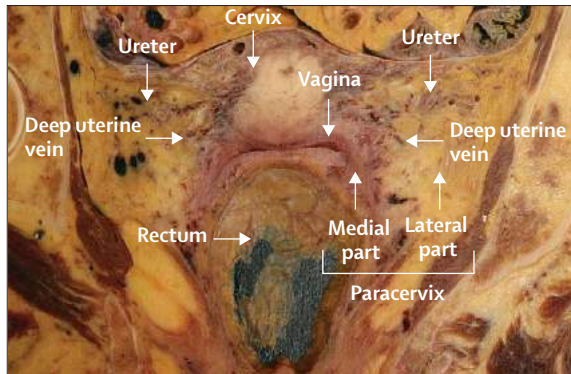


**Figure 1: Transverse section of pelvis**  
Anatomic preparation courtesy of Brigitte Mauroy, Institute of Anatomy, Lille, France.

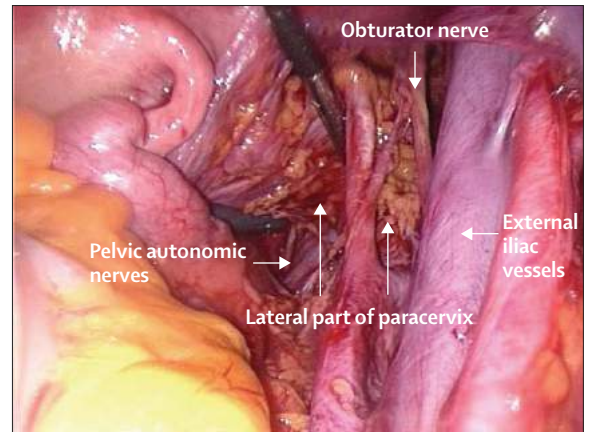
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**Figure 2:** Coronal section of pelvis of woman with history of subtotal hysterectomy  
Anatomic preparation courtesy of Brigitte Mauroy, Institute of Anatomy, Lille, France.



**Figure 3:** Operative (laparoscopic) view of paracervix after clearing of external iliac nodes

development of laparoscopic techniques and the revival of vaginal surgery.

A simpler classification has been proposed in France,<sup>17</sup> in which only two types of extended hysterectomy are defined based entirely on the lateral extent of resection: a proximal type defined as transection of the paracervix (ie, cardinal ligament) at the ureter; and a distal type defined as transection of the paracervix at the pelvic wall. The two types correspond to the modified radical and classical radical hysterectomy, respectively. However, there are drawbacks associated with this utero-centric classification. Its use has spread only among French gynaecological oncologists. It does not adapt to the trend toward reduced radicality in very early cervical cancer, or to the necessary tailoring of radicality after neoadjuvant chemotherapy or radiochemotherapy (which are being increasingly used in the management of advanced cervical cancer). Consistent with the Piver–Rutledge–Smith classification,<sup>5</sup> the French classification<sup>17</sup> ignores nerve-sparing techniques. However, it has led to a generalised classification that is independent of surgical approach (ie, abdominal or vaginal), and it recognises that oncological issues and radicality are more important than any other consideration, including the choice of minimum-access techniques. A similar idea has been used by Italian surgeons to try to develop a general classification of radical hysterectomy, who defined three classes from a less-than-radical hysterectomy to that of a radical hysterectomy.<sup>18</sup>

Another sophistication of the idea of proximal versus distal resection was the development of paracervical lymphadenectomy.<sup>19</sup> The rationale of this technique is that the lateral part of the paracervix (cardinal ligament) is essentially made of cellulolymphatic tissue, vessels, and nerves, thus the node-bearing tissue can be removed in a way that is similar to that of a lymph-node dissection, while preserving the vessels and nerves. Addition of a lateral paracervical dissection to a proximal-type radical hysterectomy improves lateral radicality and fulfills the

needs of a distal-type radical hysterectomy without increasing morbidity.<sup>19</sup> The clearing of the lateral part of the cardinal ligament has also been proposed by use of liposuction techniques in Germany<sup>20</sup> and earlier in Japan (Fujiwara 1964, Noriaki Sakuragi, University of Hokkaido, Japan, personal communication).

Figure 1 shows the paracervix at a level that includes the paracolpos. The paracervix has two parts: the medial part is a condensation of connective tissue; and the lateral part is made of fatty tissue that contains lymph nodes and surrounds vessels and nerves. The most stable anatomical landmark that marks the limit between these two parts is the terminal ureter. Figure 2 shows the paracervix, including the paracolpos of the upper third of the vagina. Its unique structure is made of condensed fibrous tissue medially and cellulolymphatic tissue laterally. The deep uterine vein is a visible landmark between the vascular and nervous components. Anatomically, the nervous component is the inferior hypogastric plexus that crosses the paracervix.

The part of the cardinal ligament that is medial to the ureter is mainly fibrous, whereas the part that is lateral to the ureter is non-fibrous and similar to any area of cellulolymphatic tissue that surrounds nerves and vessels. In figure 3, the external and internal iliac arteries are visible. The internal iliac artery seen next to the retractor is at the top of the image. The ureter has been moved medially to the left of the image by use of the retractor.

The obturator nerve is a convenient although arbitrary border between two node-bearing areas: the lateral paracervical area (left untouched at this step of surgery, as seen in figure 3); and the parietal (external and internal) area. The dorsal part of the pelvic autonomic nerves is more caudal.

As can be noted from the above discussion, the current classifications of radical hysterectomy need at least an update and ideally a complete renovation. Here, we propose a basis for a new, simple, and anatomically based

classification. This classification was first presented and discussed during an international conference on radical hysterectomy, including surgical anatomy, in Kyoto, Japan, on Feb 9, 2007.

## Methods

We reviewed current literature on: techniques of radical hysterectomy; identification of basic components of classification in surgical oncology; and identification of anatomical terms for radical hysterectomy in the international anatomical nomenclature Terminologia Anatomica.<sup>21,22</sup> The authors of the most recent anatomical work on this topic<sup>23</sup> were consulted and provided anatomical preparations. We wrote to experts who have published work during the past 10 years on the technique of radical hysterectomy. We presented and discussed our classification at a conference in Kyoto, Japan, and did further consultations with worldwide experts after this discussion.

## Identification of basic components of surgical classification

There are two common measures of the outcome of radical hysterectomy. First, some adverse effects such as bladder dysfunction correlate with anatomical extent of resection and nerve preservation when the pelvic autonomic nerves are threatened as a result of the extent of resection. Second, curative effect of surgery correlates with anatomical extent of resection, but needs documentation of the balance of benefit and risks associated with the procedure. Furthermore, combination of radiotherapy or chemotherapy, or both, with radical hysterectomy might negate any real difference in the curative effect of the extent of hysterectomy while adversely affecting the frequency of complications.

A classification is not a description of a technique. It is designed to establish the surgical template, not the way the surgeon achieves the goal. However, it should include general technical guidelines when they are crucial to the success or safety of the operation. For example, there should be mention of the management of the ureter and autonomic pelvic nerves during radical hysterectomy and lymph-node dissection.

A decision has to be made about the level of detail in the description of the surgery. The more-detailed the classification, the less likely it is to be used accurately; however, such detail may improve the correlation between anatomical extent of resection and curative effect. A compromise between a detailed description of every subtype of surgery and a simplistic view of too many variants under a given category would be to refer only to categories that are relevant to the issue of tailoring radicality, returning to the basic principles of surgical oncology.

We considered the introduction or omission of the extent and radicality of lymph-node dissection. A classification of cancer surgery that does not mention

lymph-node dissection is incomplete. However, introduction of the characteristics of node dissection within the broad categories of removal of the central disease would add to the complexity. Although the level of radicality of radical hysterectomy and lymph-node dissection are strongly correlated, it seems more practical to separate clearly the description of lymph-node dissection from that of radical hysterectomy. Moreover, the classification of lymph-node dissection is not specific to cervical cancer and may be used in the description of surgical management of adnexal and endometrial malignant disease.

## Anatomical nomenclature

International anatomical nomenclature should be used where it clearly applies, which is not always the case in surgical literature and daily language. However, two applications of anatomical nomenclature need incorporation into surgeons' language because they clarify communication substantially.

First, surgeons can use incorrect anatomical terms that define spatial orientation. The widely used terms "anterior" versus "posterior", "deep" versus "superficial", and "internal" versus "external" are confusing, depending on surgical point of view. They should be replaced, respectively, by ventral versus dorsal, caudal versus cranial, and medial versus lateral.

Second, the dorsolateral attachment of the cervix is named the paracervix (from the Greek *para* meaning "along side of"; figures 1–2). This term should replace others such as cardinal ligament, Mackenrod's ligament (it is not a ligament), or parametrium. In international anatomical nomenclature, parametrium refers to tissues that surround the uterine artery between the uterine corpus and pelvic sidewall cranial to the ureter, corresponding to the superficial uterine pedicle (uterine artery and superficial uterine vein) and related connective tissue and lymph channels. Moreover, the structure named by surgeons as paracolpos or paracolpium is included in the paracervix in the international anatomical nomenclature. The lateral attachments of the bladder and rectum are named lateral ligament of the bladder and rectum, respectively.

The term "meso" is strictly limited to the peritoneal attachment of intra-abdominal viscera. The so-called mesoureter is a sheet of connective tissue that extends dorsally from the ureter and contains the superior hypogastric nerve. The latter should be preserved during radical hysterectomy and during common iliac and aortic dissection if a nerve-sparing technique is considered. By contrast, the term "mesometrium" (or the term "mesorectum" widely used by rectal surgeons) refers to a functional view of cancer spread based on embryological development.<sup>24</sup> Therefore, only the purely descriptive term "paracervix" will be used in the surgical classification.

The pelvic autonomic nerves have been described thoroughly in the anatomical and surgical literature.<sup>10,12,23</sup>



**Figure 4: Type A radical hysterectomy**  
Same anatomical preparation as shown in figure 1. Border shows area of resection.

Because nerves cannot be shown on anatomical gross sections as those given in this Personal View, the most recent work on this topic, including dissections, is by Mauroy and colleagues.<sup>23</sup> Throughout the classification, the term “nerve preservation” will refer to specific surgical steps to identify the hypogastric nerves, the inferior hypogastric nerve plexus, and its bladder branches, allowing resection of oncologically relevant pericervical structures while preserving the sympathetic and parasympathetic innervation of pelvic organs. The anatomical localisation of the nerves is another way to describe the contents of the paracervix, with its cranial (anterior, superficial) vascular and cellulolymphatic component and its caudal (posterior, deep) neural component. The deep uterine vein may be used as a landmark between the two components.

However, there are drawbacks to the strict use of Terminologia Anatomica. Some structures relevant to surgical considerations, including the paracolpos or paracolpium, are not officially recognised. Anatomists do not consistently abide by their own rules: for example, routine description of the superior and inferior hypogastric nerves, or of the superficial and deep uterine veins. However, the use of some surgical terms will probably remain because they refer to structures that are created by surgical dissection. First, the so-called bladder pillar (otherwise referred to as ventral or anterior parametrium) is defined after surgical opening and developing of the vesicouterine septum (vesicocervical and vesicovaginal spaces) and paravesical spaces. The bladder pillar is split into a medial and lateral portion (component or leaf) by the ureter, respectively, corresponding to the vesicouterine ligament and the lateral ligament of the bladder. Second, the so-called rectal pillar (otherwise referred to as dorsal or posterior parametrium) is defined after surgical opening of the rectovaginal septum and pararectal spaces. The rectal pillar corresponds to the uterosacral ligament plus the rectouterine and rectovaginal ligament. It can be separated surgically from the hypogastric nerve that runs lateral to it.<sup>11,25</sup>

To simplify anatomical nomenclature for the radical-hysterectomy classification, we will use consistently the terms “paracervix”, “vesicouterine ligament”, and “uterosacral ligament” for the structures usually named by surgeons, respectively, as lateral parametrium (or cardinal ligament), anterior parametrium, and posterior parametrium.

### Proposed classification

For simplification, the classification is based on only the lateral extent of resection. However, given the correlation between the lateral, dorsal, and ventral extents of resection, a description of dorsal and ventral templates is added. Vaginal resection is mentioned only as a modifiable component adapted to vaginal extension of disease and any associated vaginal intraepithelial neoplasia. Vaginal lengths that are given are thus only indicative and arbitrary, and do not affect the surgical classification. Management of the ureter—an essential feature of radical hysterectomy and a potential source of major complications—is described for every type of resection.

Only four types of radical hysterectomy are described, adding when necessary a few subtypes. Relatively stable anatomical landmarks are used to define the limits of resection, such as the crossing of the ureter with the uterine artery and paracervix, and the vascular plane of the internal iliac system. To make a clear distinction with the Piver–Rutledge–Smith current classification,<sup>5</sup> letters are used rather than numbers to define classes. Simple hysterectomy is not included in the classification. Lymph-node dissection, an essential part of surgical management of cervical cancer,<sup>2</sup> is considered separately.

#### Type A: minimum resection of paracervix

This resection is an extrafascial hysterectomy, in which the position of the ureters is determined by palpation or direct vision (after opening of the ureteral tunnels) without freeing the ureters from their beds (figure 4). The paracervix is transected medial to the ureter, but lateral to the cervix. The uterosacral and vesicouterine ligaments are not transected at a distance from the uterus. Vaginal resection is generally at a minimum, routinely less than 10 mm, without removal of the vaginal part of the paracervix (paracolpos).

The aim of surgery is to ensure that the cervix is entirely removed. This issue is crucial for the design of future trials to assess the safety of a reduction in radicality for the management of early invasive cervical cancer (ie, <2 cm) with negative pelvic lymph nodes and without invasion of the lymph vascular space (based on a low prevalence of pericervical involvement in small cancers),<sup>1,26</sup> and for the final surgical management of advanced cervical cancer after radiotherapy or chemotherapy (or both). The described management of the ureter is added to avoid mechanical or thermal injury to the ureter, while avoiding impairment of the vascular supply to the terminal ureter.



**Figure 5: Type B1 radical hysterectomy**  
Same anatomical preparation as shown in figure 1. Border shows area of resection.

#### **Type B: transection of paracervix at the ureter**

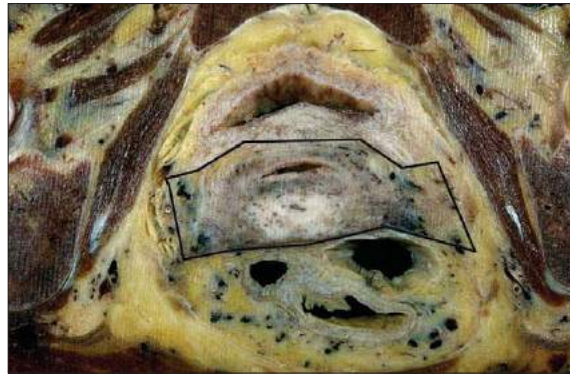
Partial resection of the uterosacral and vesicouterine ligaments is a standard part of this category (figure 5). The ureter is unroofed and rolled laterally, permitting transection of the paracervix at the level of the ureteral tunnel. The caudal (posterior, deep) neural component of the paracervix caudal to the deep uterine vein is not resected. At least 10 mm of the vagina from the cervix or tumour is resected.

The operation corresponds to the modified or proximal radical hysterectomy and is adapted to early cervical cancer. The radicality of this operation can be improved without increasing postoperative morbidity by lymph-node dissection of the lateral part of the paracervix, thus defining two subtypes: B1 (as described); and B2, with additional removal of the lateral paracervical lymph nodes.

The border between paracervical and iliac or parietal lymph-node dissection is defined arbitrarily as the obturator nerve: paracervical nodes are medial and caudal (figure 3). The combination of paracervical and parietal dissections is simply a comprehensive pelvic-node dissection. However, the lateral part of the paracervix has traditionally been resected fully in so-called type III–IV or distal radical hysterectomy. Paracervical lymphadenectomy has been invented to avoid clamping of the paracervix at the pelvic wall, along with nerves and vessels, during radical hysterectomy. Paracervical lymphadenectomy is thus logically inserted in the subclassification of type B: the morbidity of type B2 does not differ from that of B1,<sup>19</sup> although the combination of B1 with paracervical lymph-node dissection may be equivalent to that of type C1 resection.

#### **Type C: transection of paracervix at junction with internal iliac vascular system**

This type is transection of the uterosacral ligament at the rectum and vesicouterine ligament at the bladder (figure 6). The ureter is mobilised completely. 15–20 mm of vagina from the tumour or cervix and the corresponding paracolpos is resected routinely, depending on vaginal and paracervical extent and on surgeon choice.



**Figure 6: Type C2 radical hysterectomy**  
Same anatomical preparation as shown in figure 1. Border shows area of resection.

Type C corresponds to variants of classical radical hysterectomy. By contrast with types A and B, in which the autonomic nerve supply to the bladder is not threatened, the issue of nerve preservation is crucial. Two subcategories are defined: C1 with nerve preservation; and C2 without preservation of autonomic nerves. In C1, the sacrouterine ligament is transected after separation of the hypogastric nerves. The nerve is identified systematically and preserved by transection of only the uterine branches of the pelvic plexus. The bladder branches of the pelvic plexus are preserved in the lateral ligament of the bladder (ie, lateral part of bladder pillar). If the caudal part of the paracervix is transected, careful identification of bladder nerves is needed.<sup>10</sup>

For C2, the paracervix is transected completely, including the part caudal to the deep uterine vein.

#### **Type D: Laterally extended resection**

This group of rare operations feature additional ultraradical procedures, mostly indicated at the time of pelvic exenteration. Type D1 is resection of the entire paracervix at the pelvic sidewall along with the hypogastric vessels, exposing the roots of the sciatic nerve.<sup>13</sup> There is total resection of the vessels of the lateral part of the paracervix; these vessels (ie, inferior gluteal, internal pudendal, and obturator vessels) arise from the internal iliac system.

Type D2 is D1 plus resection of the entire paracervix with the hypogastric vessels and adjacent fascial or muscular structures. This resection corresponds to the LEER (laterally extended endopelvic resection) procedure.<sup>14</sup>

#### **Lymph-node dissection**

Anatomically, arteries are the most-stable landmarks. Four areas or levels are defined according to corresponding arterial anatomy: level 1, external and internal iliac; level 2, common iliac (including presacral); level 3, aortic infra-mesenteric; and level 4, aortic infrarenal.

Although lymph nodes can cross borders, the limit between level 1 and level 2 is the bifurcation of the common iliac artery; the limit between level 2 and level 3 is the

**Panel: Important features of operative report for radical hysterectomy**

All parts of the definition of the type of radical hysterectomy (eg, type C must include all parts of the definition, including site of transection of pericervical tissues and vagina)

Mode of management of uterine artery, which is routinely divided at its origin from the internal iliac artery but may be divided in the broad ligament in type A or resected with vessels in type D

Surgical and pathological length of ventral, dorsal, and lateral extent of resection: surgical length should be measured on a fresh sample without stretching; pathological length should be measured after fixation; and measurements should be taken independently from the surgeon

Surgical and pathological minimum length of vagina removed and, when applicable, minimum distance between tumour and section margin: surgical length should be measured on a fresh sample without stretching; pathological length should be measured after fixation; and measurements should be taken independently from the surgeon

Approach used, with separate consideration of approach for radical hysterectomy and that of lymph-node dissection (ie, open abdominal, vaginal, laparoscopic, vaginal with preliminary laparoscopic steps, laparoscopic with preliminary vaginal steps, or robotic)

Use of preoperative external radiotherapy, brachytherapy, or chemotherapy, or any combination of techniques

bifurcation of the aorta; and the limit between level 3 and level 4 is the inferior mesenteric artery. This classification ignores the widely used pelvic versus aortic dissection, considering that the limit of the pelvis is somewhere within the common iliac area. It also avoids the use of the term “interiliac” that describes the clearing of the area between the external and internal iliac artery. Although the term is convenient, neglecting the removal of lateral external iliac nodes might be unsafe, and there is no evidence that inclusion of the lateral nodes in the dissection increases the morbidity of lymph-node dissection.

Another issue is the limit between paracervical lymphadenectomy, which is part of radical hysterectomy, and that of internal lymph-node dissection. The arbitrary landmark is the obturator nerve. Tissues that are medial and caudal to the obturator nerve are classified as paracervix; tissues that are cranial and lateral to the obturator nerves are classified as iliac.

Within every level, and independently from each other, several types of lymph-node dissection must be defined to describe adequately the radicality of the procedure: diagnostic (minimum sampling of sentinel node only, removal of enlarged nodes only, or random sampling); systematic lymph-node dissection; and debulking (resection of all nodes >2 cm).<sup>27</sup>

**Discussion**

It is a challenge to integrate into a generalised classification a universally accepted anatomy, all subtypes of surgery that have been reported, the various ideas of radicality supported by descriptive anatomy or embryology, and variable margin requirements according to tumour size and location. Furthermore, some surgery might be asymmetrical (eg, type C1 or B on one side and type C2 on the opposite).

However, it must be accepted that every effort to simplify categories requires a renouncement to include personal anatomical interpretation, technical details, and ideas.

It is not possible to describe all individual operations, and the use of a simple classification does not preclude careful description of an operation. A list of required information should be part of any quality control in surgical management of cervical cancer. The panel summarises what should be included in an operative report.

Moreover, achievement of haemostasis must be defined to aid assessment of new techniques or devices in terms of radicality and outcome such as blood loss or complications. Moreover, achievement of lateral resection depends on haemostasis technique,<sup>28</sup> which highlights the importance of technical improvements irrespective of classification and the need for a precise technique and description of the technique used in the operative report.

A tumour–node–metastasis-type description of the operation that defines three classes of radicality in the ventral, dorsal, lateral, and deep lateral directions might be developed (Trimbos JB, University of Leiden, Netherlands, personal communication). If confirmed, a proposed embryological basis for the mesometrium<sup>24</sup> might give insight into the rationale of lateral extent of radical hysterectomy. This basis clearly separates Müllerian structures that need systematic resection from the vesical and rectal attachments that are thought to be safe at least in the early stages of cancer. This idea does not contradict our classification; rather, it adds a potential interpretation of tumour margin, with the assumption that a 1-cm margin is not necessary outside the limits of the Müllerian compartment. However, this assumption does not modify the need for a margin in the Müllerian compartment, in the paracervix, and in the vagina.

The adoption of fertility-preserving surgery after the invention of the Dargent operation<sup>16</sup> has led inevitably to variants in approach and radicality. The Dargent operation<sup>16</sup> corresponds to a type-B radical surgery in our classification. More recently, new variants adapted for treatment of minimal disease or after neoadjuvant chemotherapy have been described and correspond to type A radical surgery. For all patients, information on pathological distance between the tumour and the endocervical resection margin must be added to the standard list of requirements.

Radical hysterectomy is not a single type of operation: variations must balance curative effects with the risk of adverse consequences. An internationally accepted classification of radical hysterectomy, as we propose here, with the goal of acceptance by individual surgeons, study groups, and by national and international societies is clearly needed. Future randomised studies will need to be large-scale to confirm available evidence from smaller studies<sup>29</sup> and to answer new questions. In the future, assessment of techniques and quality control will be a basic part of every surgery.

### Search strategy and selection criteria

We searched PubMed using the terms: "radical hysterectomy technique"; "radical hysterectomy classification"; "radical hysterectomy tailoring" for studies between January, 1970, and March, 2007. Only papers in English relevant to the topic were selected; reviews were excluded. The personal collection of one of the authors (DQ) was used to search historical early publications. Material in Japanese was provided by Noriaki Sakuragi, Sapporo, Japan.

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### Conflicts of interest

The authors declared no conflicts of interest.

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