


OSPEDALE
CANNIZZARO
Fondazione per la Ricerca e la Cura


Azienda Ospedaliera
Cannizzaro

U.O. di Ostetricia e Ginecologia

Direttore: Prof. Paolo Scollo

**Centro di Riferimento Regionale
per l'Oncologia Ginecologica**

GURS n. 53 del 14/12/2012

Azienda Ospedaliera "Cannizzaro"
Catania

Dipartimento Materno-Infantile
U.O. di Ostetricia e Ginecologia
Direttore: prof. Paolo Scollo



Associazione
Italiana
Radioterapia
Oncologica

XXIII CONGRESSO
AIRO

Giardini Naxos - Taormina, 26 - 29 ottobre



**Carcinoma della portio:
Chirurgia vs Radioterapia negli stadi
iniziali:
"Il punto di vista del chirurgo"**

Giardini Naxos 26/10/2013



XXIII CONGRESSO
AIRO2013

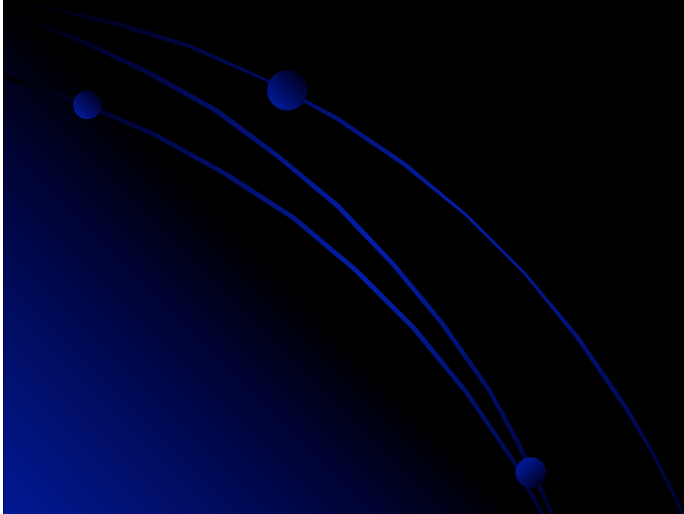
Taormina, 26-29 ottobre
Giardini Naxos

DICHIARAZIONE

Relatore: Paolo Scollo

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

Non ho conflitti di interessi



Talk Plan

- Epidemiologia
- Prevenzione e lesioni precancerose
- Strategie nel cancro negli stadi iniziali:
 - Chirurgia radicale
 - Complicanze
 - Trattamento conservativo
 - Trattamento adiuvante
- Strategie nel cancro localmente avanzato
- Futuro

dalla formazione alla ricerca

nuove frontiere nei trattamenti
medici e chirurgici
in ginecologia oncologica



22 congresso nazionale società italiana di oncologia ginecologica

CATANIA 5/7 LUGLIO 2010
EXCELSIOR GRAND HOTEL

7 Luglio V SESSIONE CARCINOMA DELLA CERVICE UTERINA

08.30 - 09.00

Lettura magistrale

L'evoluzione della chirurgia radicale nel cervico-carcinoma
H. Tulusan

Presidente

F. Raspagliesi

Moderatori

D. Gueli-Alletti, A. Maneo, F. Maneschi

09.00 - 09.20

La vaccinazione contro l'HPV:
up-to-date

G. Pasciullo

09.20 - 09.40

Trattamento delle precancerose cervicali:
quale tecnica e quale outcome

G. Scibilia

09.40 - 10.00

Terapia conservativa nel cancro cervicale
invasivo: quando e quale protocollo

F. Landoni

10.00 - 10.20

Cervicocarcinoma localmente avanzato:
up-to-date su chemioterapia
neoadiuvante e chirurgia radicale
vs radio-chemioterapia

PL. Benedetti Panici

10.20 - 10.40

Chemioterapia di consolidamento dopo
chemioterapia neoadiuvante e chirurgia
radicale: pro e contro

S. Greggi

10.40 - 11.00

La TC/PET nel management del
cervicocarcinoma inoperabile

M. Ippolito

11.00 - 11.15

Coffee break

SABATO, 18 GIUGNO 2011

Cancro
della
cervice
UP
TO
Date

AZIENDA
OSPEDALIERA CANNIZZARO



Trattamento
del
cancro
cervicale
avanzato

SABATO
18 GIUGNO
2011
AZIENDA
OSPEDALIERA
CANNIZZARO



100% of cervical cancers are caused by HPV



Global total HPV-attributable cancers in 2002

Site	Total cancers	Attributable to all HPV		Attributable to HPV 16/18	
		Cases	% HPV cancer	%	Cases
Cervix	492,800	492,800	93.5	70+	344,900
Vulva, vagina	40,000	16,000	3	80	12,800
Anus	15,900	14,300	2.7	92	13,100
Oropharynx	9,600	1,100	0.2	91	1,000
Mouth	98,400	2,900	0.5	97	2,800
Total		527,100			374,600

Adapted from Parkin DM & Bray F. *Vaccine* 2006; **24**(Suppl 3):S11.
Walboomers JMM, et al. *J Pathol* 1999; **189**:12–19.

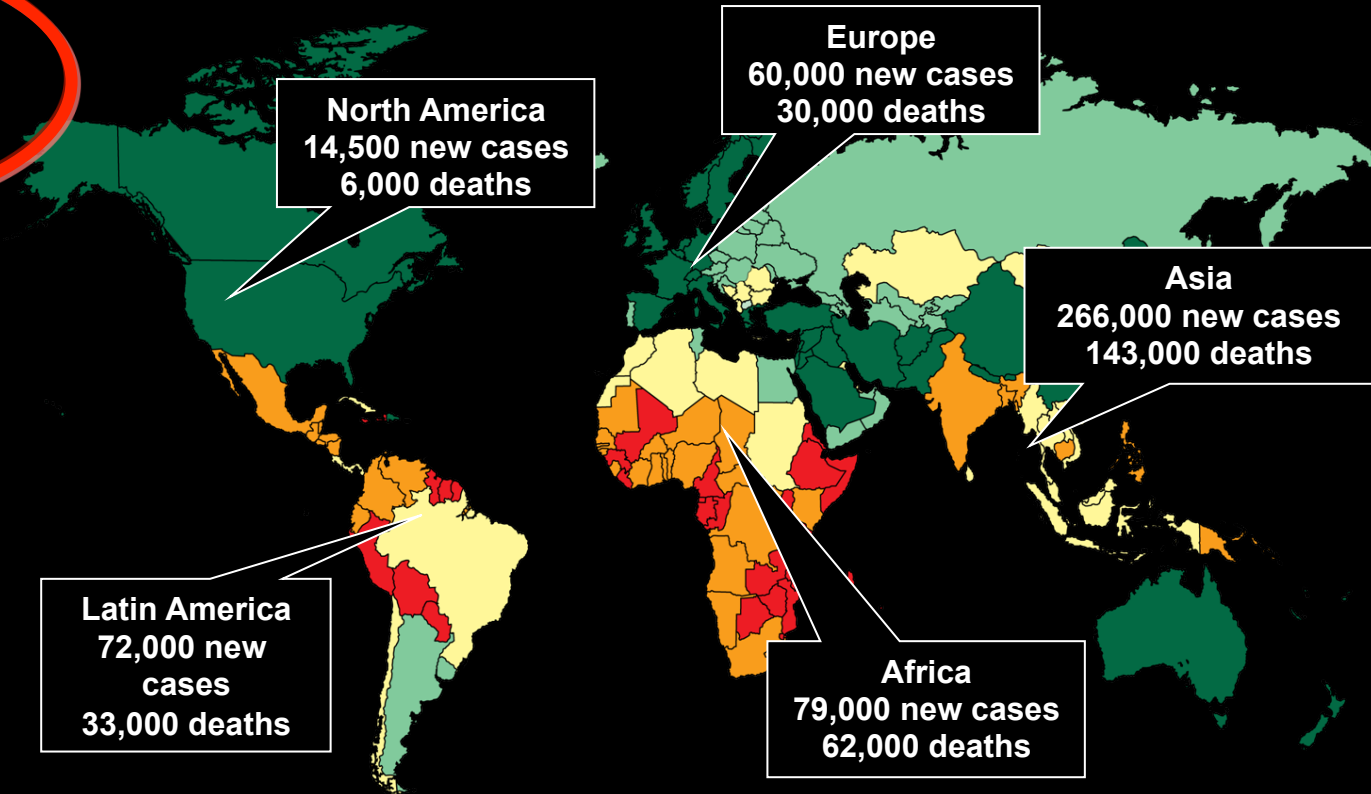
Global mortality per annum



Worldwide, every 2 minutes a woman dies of cervical cancer¹

The highest burden of disease (up to 80%) occurs in less developed regions¹ where there is a lack of effective screening programmes

This demonstrates a clear medical need for new cervical cancer interventions



Cervical cancer mortality rates worldwide
Cases per 100,000 women per year

1. Ferlay J, et al. GLOBOCAN 2002 Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase; Lyon, 2004.

Invasive cervical Cancer

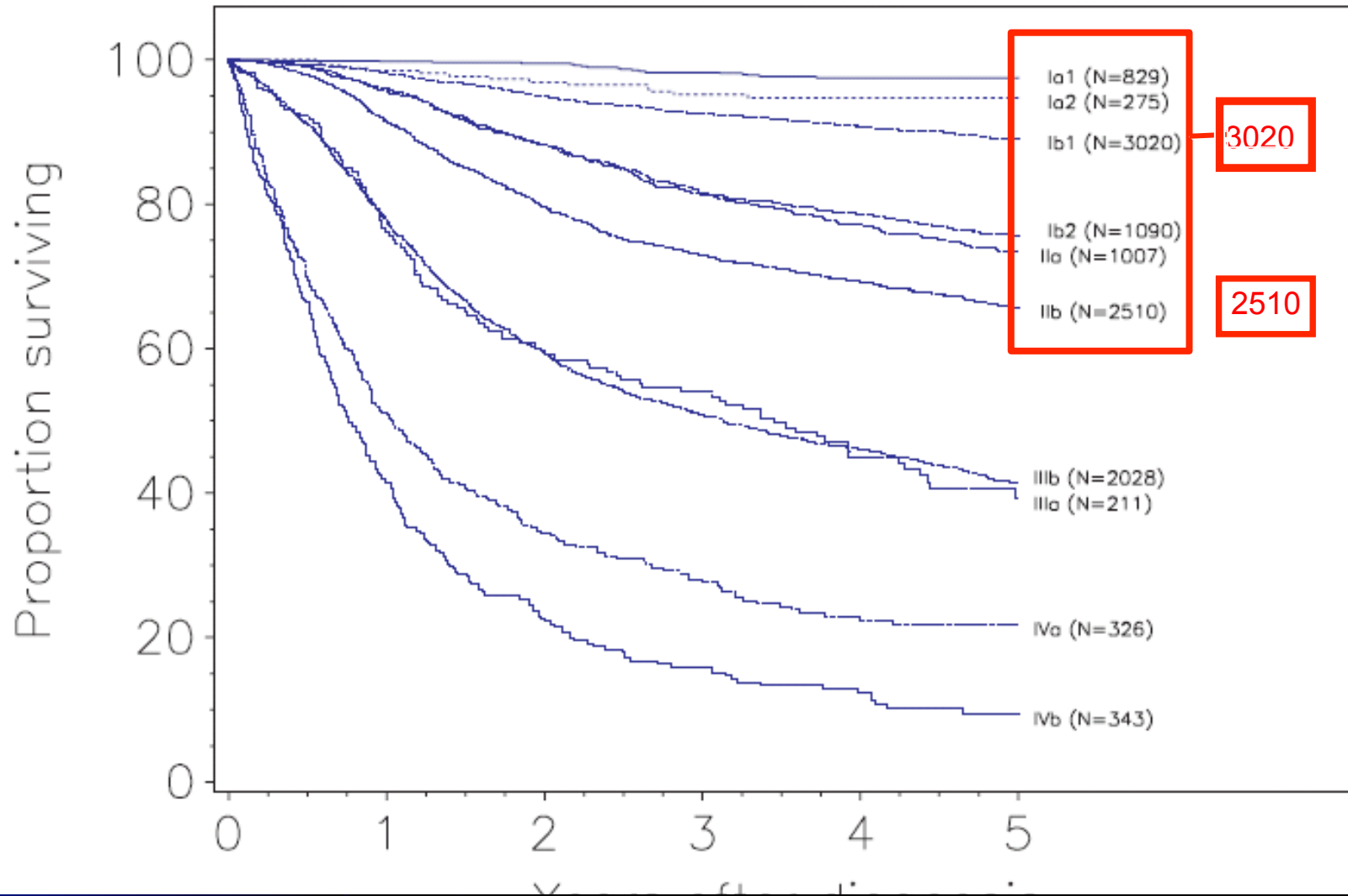
Cervical cancer in the world

- ❑ Second cause of cancer death in women
- ❑ Leading cause in many developing countries
- ❑ 530,232 cases and 275,008 deaths in 2008
- ❑ Incidence varies dramatically with the availability of screening

26th Annual Report 2006

(patients treated 1999-2001)

MA QUINN, JL BENEDET, *et al*





Il modo migliore di guarire è
"non ammalare"

Prevenzione primaria
Prevenzione secondaria



Cancro cervice invasivo in Italia:

3700 nuovi casi ogni anno

4% di tutti i tumori ginecologici

1700 morti ogni anno

Displasia cervicale in Italia

14.700 nuovi casi/anno di H-SIL

47.000 nuovi casi/anno di L-SIL

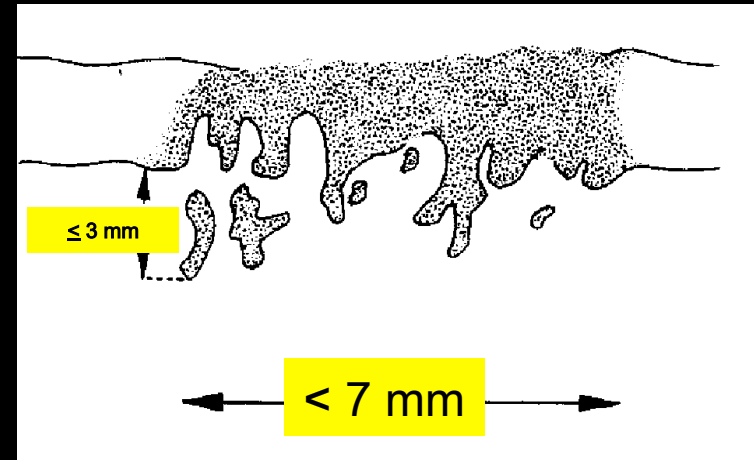
92.000 nuovi casi/anno di ASC-US

153.000 nuovi casi da gestire

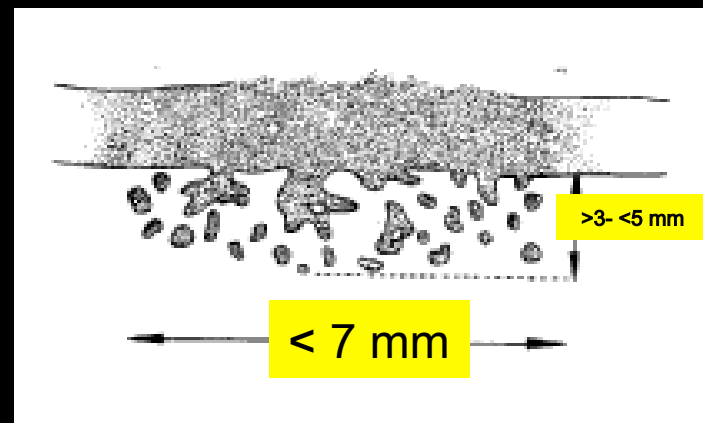
STADIAZIONE

Carcinoma invasivo

- Carcinoma microinvasivo (Stadio FIGO Ia1)

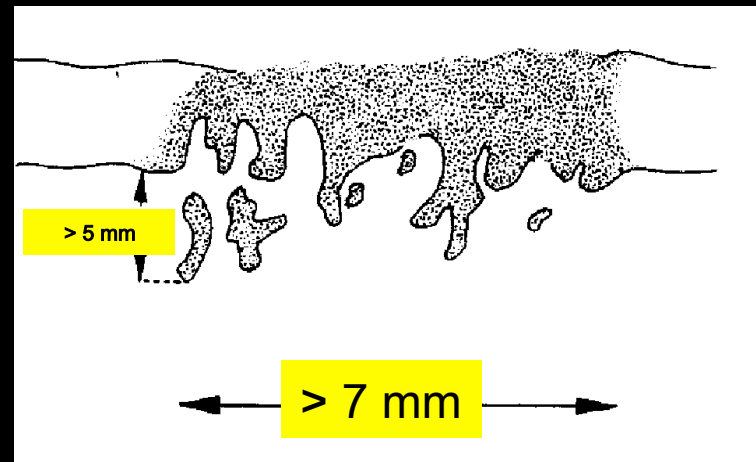


- Carcinoma microinvasivo (Stadio FIGO Ia2)



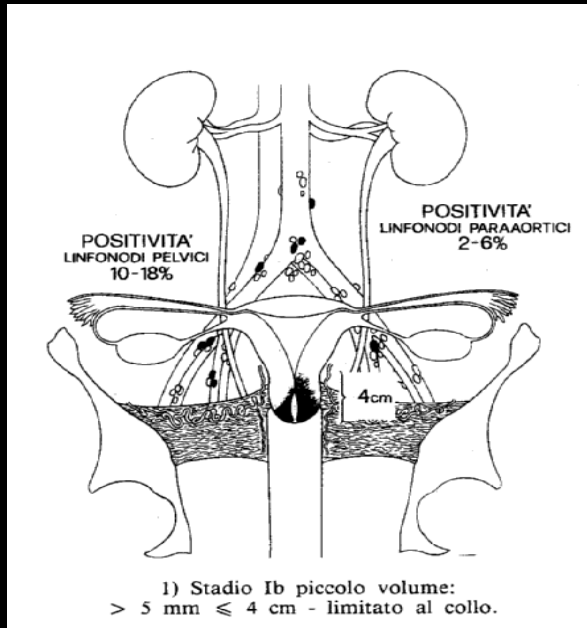
Carcinoma invasivo

- Carcinoma invasivo
(Stadio FIGO Ib1-IV)

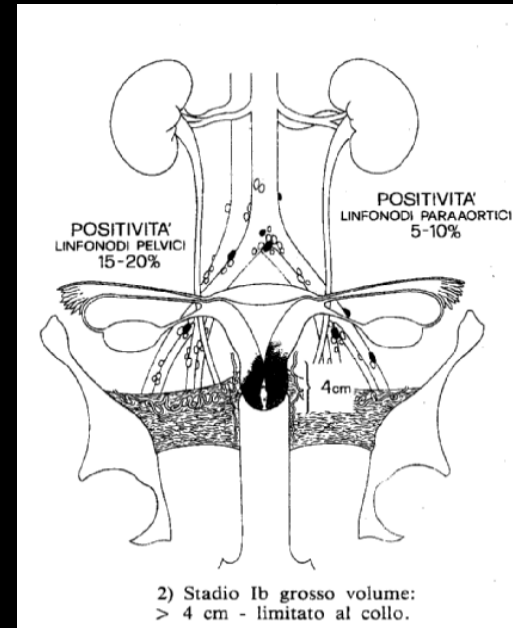


Stadiazione FIGO...

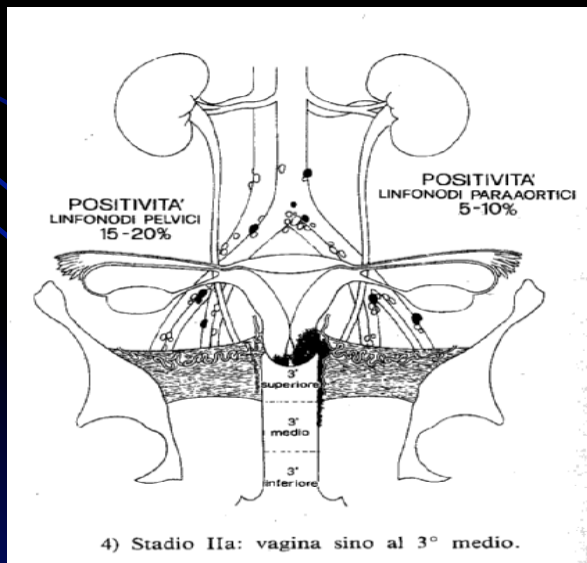
Stadio IB1



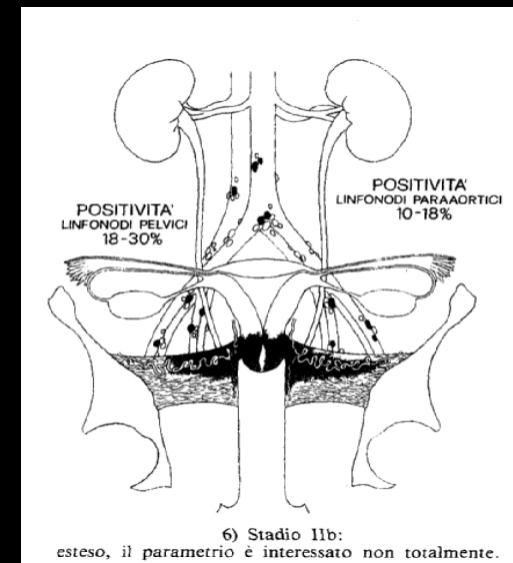
Stadio IB2



Stadio IIA1-2

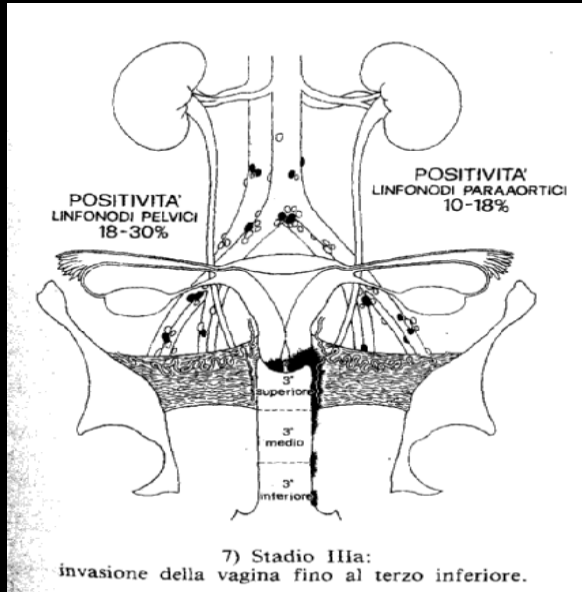


Stadio IIB

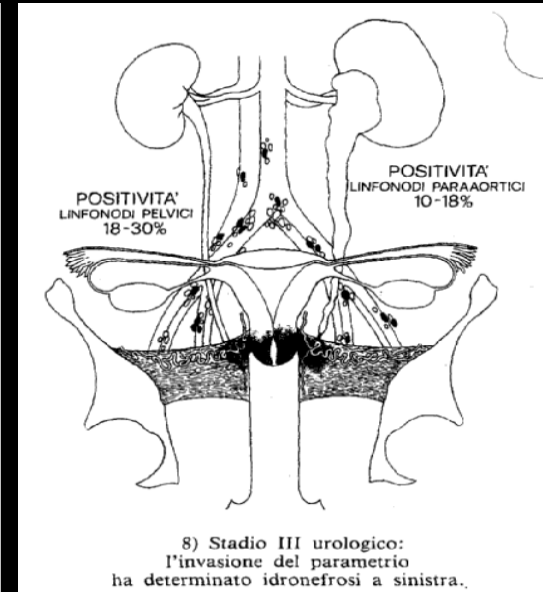


Stadiazione FIGO

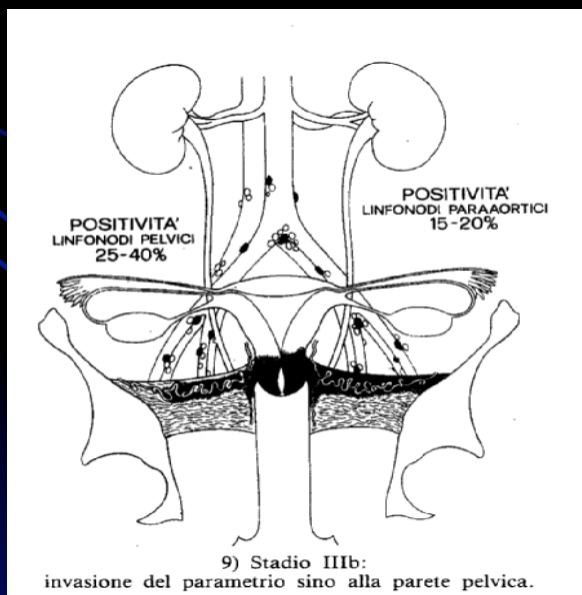
Stadio
IIIA



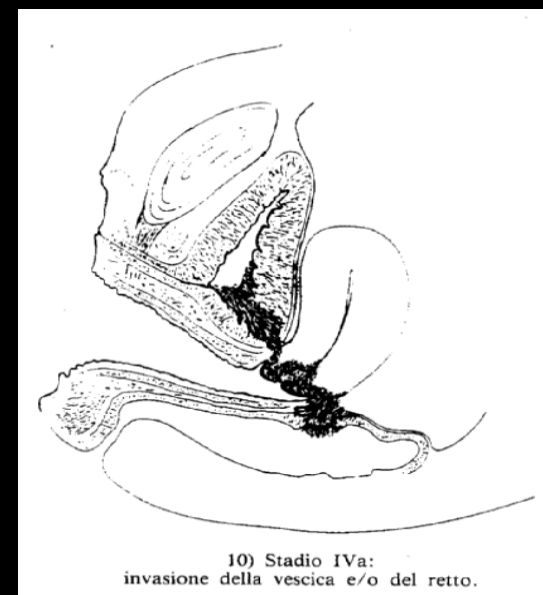
Stadio IIIA



Stadio
IIIB



Stadio IVA



SOPRAVVIVENZA

<i>Stadio</i>	<i>% Sopravvivenza 5 anni</i>
Ia1-2	97-100
Ib	77-95
IIa	75-95
IIf	57-78
III	46-50
IV	0-16

trattamento conservativo
o demolitivo

<i>LINFONODI</i>	<i>% Sopravvivenza 5 anni</i>
PELVICI POSITIVI	56-65% (STADIO IIf)
AORTICI POSITIVI	9-40%



Nuova classificazione/ stadiazione

FIGO

International Federation of



Gynecology and Obstetrics

Recommendations from FIGO Gyn Onco Committee - 1

- Surgical staging is not practical or feasible or beneficial in the majority of cervical cancer patients and hence it is not recommended for staging
 - ***Cervical cancer should remain a clinically staged disease***
- Pathological extent and other pathological findings (such as LVSI) if available should be reported to the FIGO Annual Report or in scientific publications
- Use of imaging, such as MRI, if available, in the assessment of the size of primary tumour is encouraged but not mandatory

CERVIX UTERI CANCER

Carcinoma of the cervix uteri (FIGO 2009)

Stage 0	Deleted
Stage I	The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded). Invasive carcinoma which can be diagnosed only by microscopy.
IA	All macroscopically visible lesions – even with superficial invasion – are allotted to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5.00 mm and a horizontal extension of not > 7.00 mm. Depth of invasion should not be > 5.00 mm taken from the base of the epithelium of the original tissue – superficial or glandular. The involvement of vascular spaces – venous or lymphatic – should not change the stage allotment.
IA ₁	Measured stromal invasion of not > 3.0 mm in depth and extension of not > 7.0 mm.
IA ₂	Measured stromal invasion of > 3.0 mm and not > 5.0 mm with an extension of not > 7.0 mm.
IB	Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA.
IB ₁	Clinically visible lesion ≤ 4.0 cm in greatest dimension.
IB ₂	Clinically visible lesion > 4.0 cm in greatest dimension.
Stage II	Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina.
IIA	Without parametrial invasion.
IIA ₁	Clinically visible lesion ≤ 4.0 cm in greatest dimension.
IIA ₂	Clinically visible lesion > 4 cm in greatest dimension.
IIB	With obvious parametrial invasion.
Stage III	The tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney.*
IIIA	Tumor involves lower third of the vagina, with no extension to the pelvic wall.
IIIB	Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney.
Stage IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to Stage IV.
IVA	Spread of the growth to adjacent organs.
IVB	Spread to distant organs.

* On rectal examination, there is no cancer-free space between the tumour and the pelvic wall. All cases with hydronephrosis or non-functioning kidney are included, unless they are known to be due to other cause.

Quale stadio di malattia ?

E quindi

Quale trattamento del
cancro ?

Cervical cancer: Therapeutic strategy

0 → IIA Surgery and/or radiotherapy

IIB → IV A Chemo-RT

Chemo-surgery +/- RT

IVB- rec. Chemotherapy



Carcinoma invasivo preclinico (Stadio FIGO I A1 $\leq 3\text{mm}$)

1. Conizzazione (margini liberi)

2. Isterectomia extrafasciale

0% di invasione linfatica

Non linfadenectomia



Sopravvivenza 5 anni: 98-100%

**Carcinoma invasivo preclinico
(Stadio FIGO I A2 $\leq 5\text{mm}$)**

**1. Isterectomia radicale PIVER II / tipo B1-2
sec. Querleu-Morrow
con linfadenectomia pelvica**

2. Trachelectomia + linfadenectomia pelvica



Linfonodi positivi 5-8%

Sopravvivenza 5 anni: 95-98%

Carcinoma invasivo (Stadio FIGO I B1 < 4 cm)

1. Isterectomia radicale sec. Piver III +/- nerve sparing / tipo C1-C2 sec. Querleu-Morrow con linfadenectomia pelvica

2. Chemio-radioterapia



Sopravvivenza 5 anni:	95% se N-
	57 % se N+

Vol 350 • August 23, 1997

THE LANCET

Articles

Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer

Fabio Landoni, Andrea Maneo, Alessandro Colombo, Franco Placa, Rodolfo Milani, Patrizia Perego, Giorgio Favini, Luigi Ferri, Costantino Mangioni



Radical hysterectomy vs. radiotherapy in stage IB

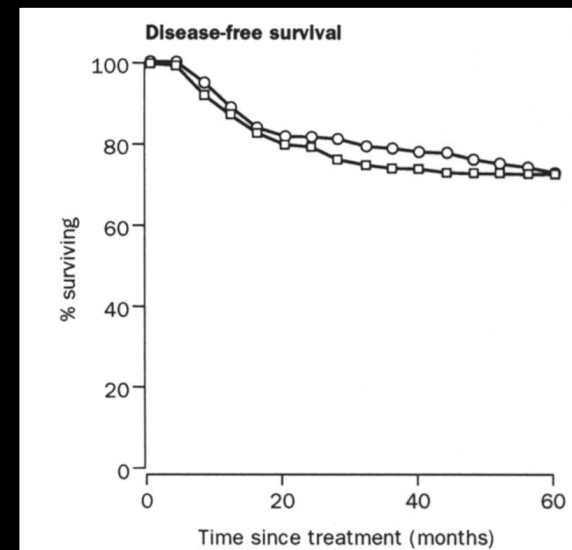
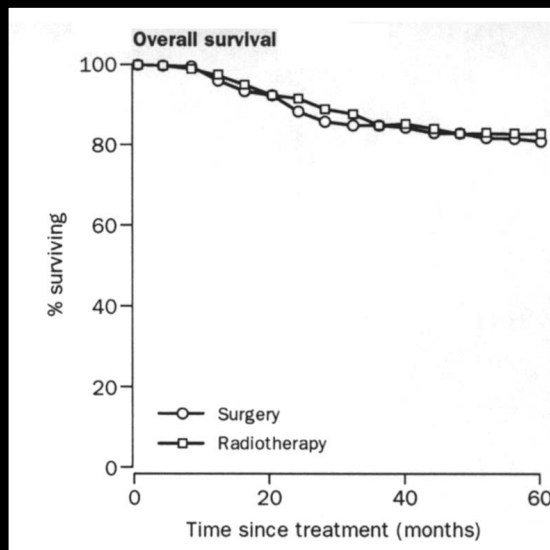
Prospective randomized study, stage IB or IIA, radical surgery vs. RT

- 343 women, 172 surgery and 171 radiotherapy
 - Surgery (Piver III) + Adjuvant RT in pT2b or bigger, margin < 3 mm, or positive lymph nodes
 - 54% patients IB1 and 84% IB2 (total 64% of surgery group)
 - Arm RT, only 72 Gy to point A
 - **OS and DFS did not differ significantly** (surgery performs better in adenocarcinoma)



Morbidity

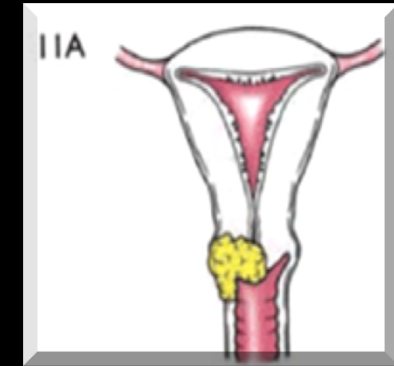
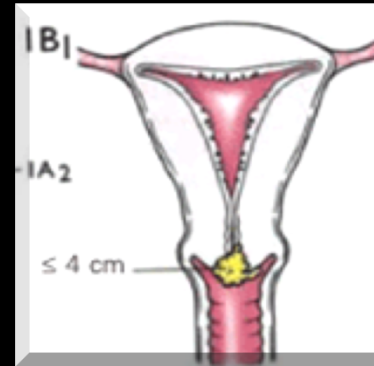
- Surgery group 28% (grade 2-3)
- Radiotherapy group 12%



Per gli stadi compresi tra **IB e IIA** sono state utilizzate la terapia chirurgica o radioterapica con risultati simili....

Lo studio di Landoni et Al. (1997 Lancet), non evidenziava differenze in termini di DFS e OS in pazienti agli stadi FIGO IB e IIA trattati con chirurgia o radioterapia...ma alle pazienti con "bulky tumors" nel braccio chirurgia veniva somministrata anche radioterapia adiuvante.

Stage IB1- IIA1




- **Surgery** offers advantages for treating the younger patients:
 - preserves gonadal function
 - avoids vaginal atrophy
 - avoids psychological problems ("tumor removed")
 - avoids irreversible long-term complications.
- Aged patients treated by radiotherapy show low morbidity rate.
- The highest urological morbidity has been observed when radiotherapy is associated to surgery.

NIH Consensus Statement on Cervical Cancer Bethesda 1996


"...patients with stage IB and IIA cervical cancer are appropriately treated with either radical hysterectomy with pelvic lymphadenectomy or radiation therapy with equivalent result.

To minimize morbidity, primary therapy should avoid the routine use of both radical surgery and radiation therapy. The combined use of radical surgery and radical radiation therapy results in high morbidity and cost."

Talk Plan

- **Epidemiologia**
 - **Prevenzione e lesioni precancerose**
 - **Strategie nel cancro negli stadi iniziali:**
 - **Chirurgia radicale**
 - **Complicanze**
 - **Trattamento conservativo**
 - **Trattamento adiuvante**
 - **Strategie nel cancro localmente avanzato**
 - **Futuro**
- 

How radical should surgery be?

- Radical hysterectomy is not a single operation
 - Many variations exist for which there is no standard terminology and no standard description
- 

Five Classes of Extended Hysterectomy for Women With Cervical Cancer

M. STEVEN PIVER, MD, FACOG, FELIX RUTLEDGE, MD, FACOG
and JULIAN P. SMITH, MD, FACOG

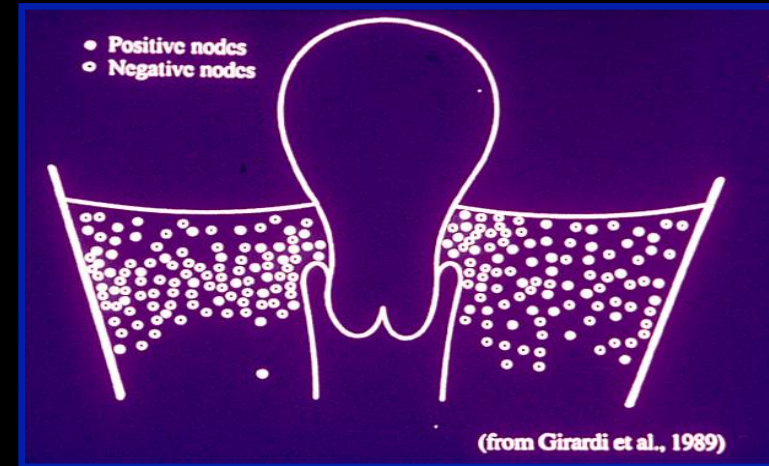
Obstet Gynecol Vol. 44, Aug 1974

- Class I : TeLinde modification
- Class II :
 - The ureters are freed from paracervical position but are not dissected out the pubovesical ligaments
 - Uterine vessels are ligated just medial to the ureters; the medial half of the cardinal ligament is removed
 - Uterosacral ligament are resected midway; 1/3 vagina is removed
- Class III :
 - The ureters are freed from pubovesical ligaments (except a small lateral portion)
 - Uterine artery is ligated at the origin; cardinal ligament is resected at pelvic wall
 - Uterosacral ligament are resected at their sacral attachments; 1/2 vagina is removed
- Class IV e V : more radical procedure (also for central recurrences)

Radicality in parametrial resection

Literature data regarding the role of surgical radicality are controversial

- Girardi (1989), parametrial lymph nodes are scattered all over the parametrial tissue. Consequently radical surgery should not just transect the parametria but resect them at their lateral insertion.



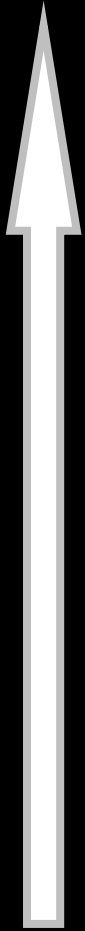
- Di Saia (1981), did not find any evidence of disease in the lateral parametria in operated patients with a stage IB or IIA lesion, suggesting lymph node metastasis occurs as an “embolic phenomenon”

% parametrial involvement in stage IB

- Burghardt and Pickel (Obstet Gynecol, 1978): parametrial involvement in 6.8% of clinical stage IB
- Delgado et al. (Gynecol Oncol, 1989): parametrial involvement in 6.8%
- Landoni et al. (Gynecol Oncol, 2001): parametrial involvement in 26%

Parametrial resection and morbidity

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Type IV

Type III

Type II

S
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Q
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A
E



Compromised
sexual function

Decreased lubrication
& genital swelling

Bladder & Bowel
dysfunction

Tailoring in cervical cancer surgery: adaptation of radicality to tumour spread

Reducing
radicality

Technical
changes

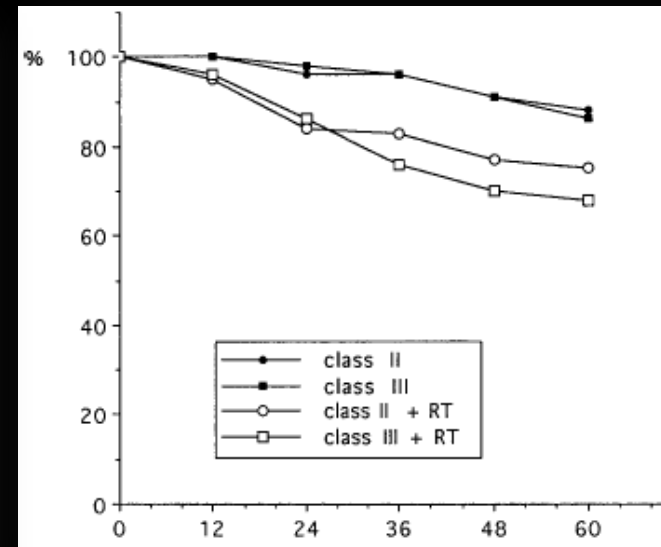
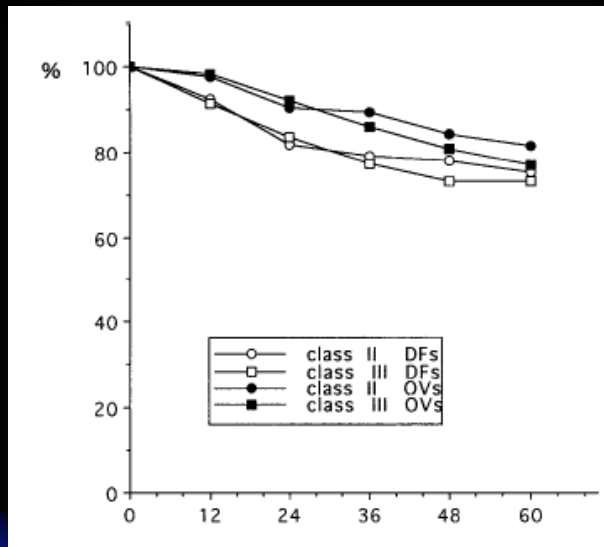
Advancement
of technology



Reducing radicality

Class II versus Class III Radical Hysterectomy in Stage IB–IIA Cervical Cancer: A Prospective Randomized Study^{1,2}

Fabio Landoni, M.D.,* Andrea Maneo, M.D.,*³ Gennaro Cormio, M.D.,† Patrizia Perego, M.D.,‡ Rodolfo Milani, M.D.,* Orlando Caruso, M.D.,* and Costantino Mangioni, M.D.*



	Class II (119 pt)	Class III (119 pt)
5-y OS	81 %	77 %
DFS	75 %	73 %
- Urologic complication surgery	5%	30%
- Urologic complication Surgery + RT	20%	37%
Adjuvant therapy (N+, P+, R+, <3mm free stroma)	64 (54%)	65 (55%)

Reducing radicality (intraoperative findings)



Available online at www.sciencedirect.com

SCIENCE @ DIRECT®

Gynecologic Oncology 96 (2005) 792–798

Gynecologic
Oncology

www.elsevier.com/locate/ygyno

Tailoring the parametrectomy in stages IA2–IB1 cervical carcinoma:
is it feasible and safe?

Pierluigi Benedetti Panici^{a,*}, Roberto Angioli^b, Innocenza Palaia^b, Ludovico Muzii^b,
Marzio Angelo Zullo^b, Natalina Mancini^b, Carla Rabitti^c

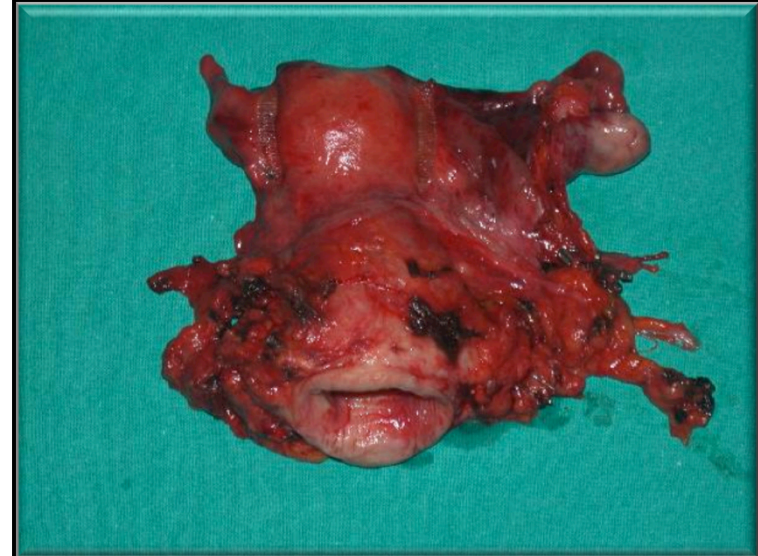
^aDepartment of Obstetrics and Gynecology, "La Sapienza" University, Viale Regina Elena 324, 00168 Rome, Italy

^bDepartment of Obstetrics and Gynecology, Campus Bio Medico University, Rome, Italy

^cDepartment of Pathology, Campus Bio Medico University, Rome, Italy

Received 1 September 2004

Available online 13 December 2004



STUDY DESIGN

SUPERFICIAL OBTURATOR, EXTERNAL ILIAC,
AND INTERILIAC NODE SYSTEMATIC LYMPHADENECTOMY

FROZEN SECTION

NODE NEGATIVE:
MODIFIED RAD. HYST.

NODE POSITIVE:
CLASSICAL RAD. HYST.

Reducing radicality (preoperative findings)



- **Retrospective** review of 200 pts with stage IB1 submitted to Piver III + plnd
- 10% of parametrial spread
- In multivariate analysis **LVSI, deep stromal invasion (>10 mm)** and **age > 50 yrs** are independent predictors of parametrial involvement (factors that could be determined by a cone biopsy)

Conclusion. Patients with a tumor depth of invasion of ≤ 10 mm, no LVSI, and aged ≤ 50 years, could be considered for less radical surgery such as modified radical hysterectomy or simple hysterectomy with pelvic lymphadenectomy.

A RANDOMIZED TRIAL COMPARING RADICAL HYSTERECTOMY AND PELVIC NODE DISSECTION VS SIMPLE HYSTERECTOMY AND PELVIC NODE DISSECTION IN PATIENTS WITH LOW RISK EARLY STAGE CERVICAL CANCER

SHAPE TRIAL

A Gynecologic Cancer Intergroup (GCIG) Trial led by the NCIC CTG

Chair: Marie Plante

studies

Author	Year	Low-risk criteria	N	Parametrial involvement in low-risk group (%)
Kinney [13]	1995	Squamous histology only, tumor <2 cm, no LVSI*	83	0.0%
Covens [14]	2002	All histologies, tumor <2 cm, DOI** <10 mm, negative pelvic lymph nodes	536	0.6%
Stegeman [15]	2007	Squamous, adenocarcinoma, adenosquamous or clear cell histology, tumor <2 cm, DOI** <10 mm, no LVSI*, negative pelvic lymph nodes	103	0.0%
Wright [16]	2008	All histologies, tumor <2 cm, no LVSI*, negative pelvic lymph nodes	270	0.4%
Frumovitz [19]	2009	Squamous, adenocarcinoma or adenosquamous histology, tumor <2 cm, no LVSI*	125	0.0%

*LVSI: lymphovascular space involvement

**DOI: depth of invasion

N=1117 < 1%

Low-risk cervical cancer as defined by:

- Stage IA2-IB1 squamous cell, adenocarcinoma/adenosquamous carcinoma
- < 2cm, at least 3mm of intact cervical stroma and < 50% stromal invasion
- Grade 1-3

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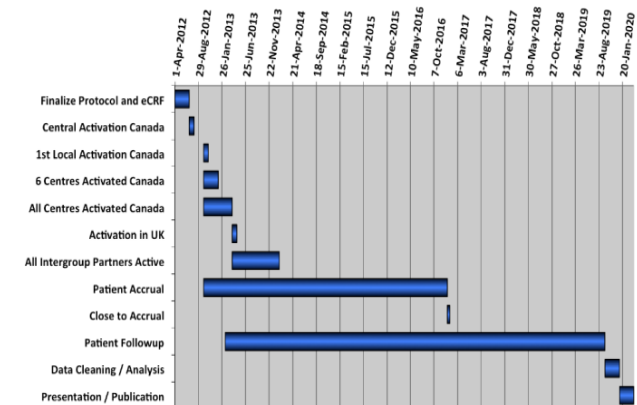
ARM 1 (Control)
Radical Hysterectomy*

ARM 2 (Experimental)
Simple Hysterectomy*

→→ Pelvic relapse

* Regardless of treatment assignment, surgery will include pelvic lymph node dissection with optional sentinel lymph node (SN) mapping. If SN mapping is to be done, the mode is optional, but the laparoscopic approach is preferred.

Planned sample size: 700 (non-inferiority at 0.05 level with 80% power)



Tailoring in cervical cancer surgery: adaptation of radicality to tumour spread

Reducing
radicality

Technical
changes

Advancement
of technology

Nerve-Sparing Radical Hysterectomy

Yabuki Y Dissection of the cardinal ligament in radical hysterectomy for cervical cancer with emphasis on the lateral ligament. Am J Obstet Gynecol 1991

Hockel M Total mesometrial resection: High resolution nerve-sparing radical hysterectomy based on developmentally defined surgical anatomy. Int J Gynecol Cancer 2003

Possover M Identification and preservation of the motoric innervation of the bladder in radical hysterectomy type III. Gynecol Oncol 2000

Trimbos JB A nerve-sparing radical hysterectomy: guidelines and feasibility in Western patients. Int J Gynecol Cancer 2001



Available online at www.sciencedirect.com

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Gynecologic Oncology 93 (2004) 307–314

Gynecologic
Oncology

www.elsevier.com/locate/ygyno

Nerve-sparing radical hysterectomy: a surgical technique for preserving the autonomic hypogastric nerve

Francesco Raspagliesi, * Antonino Ditto, Rosanna Fontanelli, Eugenio Solima, Francesco Hanozet, Flavia Zanaboni, and Shigeki Kusamura



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Gynecologic Oncology xx (2006) xxx–xxx

Gynecologic
Oncology

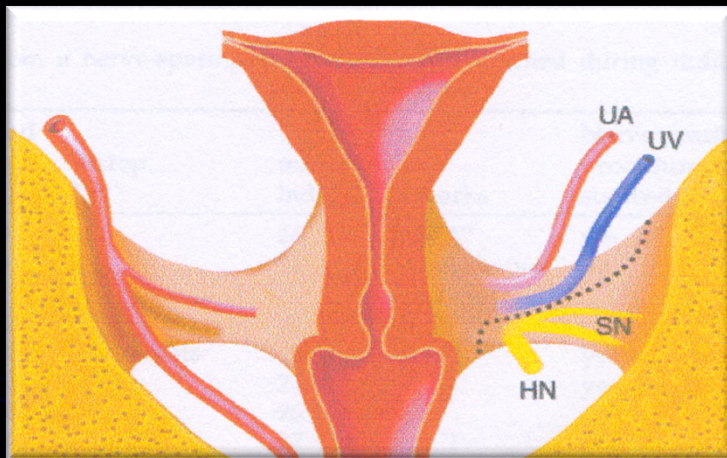
www.elsevier.com/locate/ygyno

Type II versus Type III Nerve-sparing Radical hysterectomy: Comparison of lower urinary tract dysfunctions

Francesco Raspagliesi *, Antonino Ditto, Rosanna Fontanelli, Flavia Zanaboni, Eugenio Solima, Gianbattista Spatti, Francesco Hanozet, Francesca Vecchione, Gabriella Rossi, Shigeki Kusamura

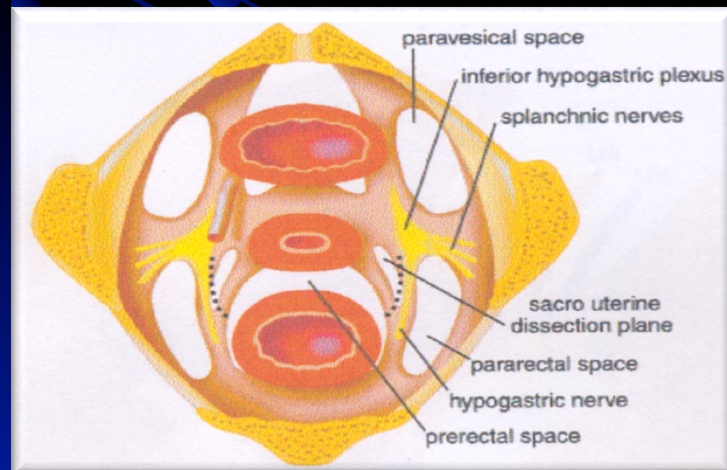
A nerve-sparing radical hysterectomy: Guidelines and feasibility in Western patients

J. B. TRIMBOS, C. P. MAAS*, M. C. DERUITER†, A. A. W. PETERS & G. G. KENTER
Department of Gynecology and † Department of Anatomy and Embryology, Leiden University Medical Center, The Netherlands



Step 1: Preserving the hypogastric nerve (and the proximal part of the inferior hypogastric plexus)

Step 2: Preserving the pelvic splanchnic nerves and middle part of the inferior hypogastric plexus



dividual anatomical situation. To avoid the inferior hypogastric plexus, the dissection follows the shape of the bow of a ship from a lateroventral to a mediodorsal position (see dotted line in Fig. 3). Through step 1,

Step 3: Preserving the distal part of the inferior hypogastric plexus



REVIEW ARTICLE

Nerve Sparing in Radical Surgery for Early-Stage Cervical Cancer

Yes We Should!

*Cornelis D. de Kroon, MD, PhD, Katja N. Gaarenstroom, MD, PhD,
Mariette I. E. van Poelgeest, MD, PhD, Alexander A. Peters, MD, PhD, and J. Baptist Trimbos, MD, PhD*

Classification of radical hysterectomy

Denis Querleu, C Paul Morrow

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.

Lancet Oncol 2008; 9:297–303

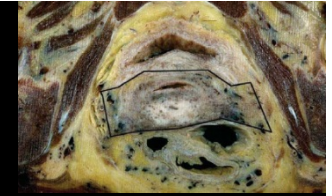
Department of Surgery,
Institut Claudius Regaud,
University Paul Sabatier,
Toulouse, France
(Prof D Querleu MD); and Keck
School of Medicine, University
of Southern California,
Los Angeles, CA, USA
(Prof C P Morrow MD)

Correspondence to:
Prof Denis Querleu, Department

- Taking into account the curative effect of surgery and adverse effects.
- Consider nerve preservation.
- Use “anatomical landmarks” (reproducibility!! ...absent in Piver et al. paper).
- Could be adapted to open, vaginal, laparoscopic or robotic surgery.



The Four Types of Radical Hysterectomy



- **Class A : minimum resection of paracervix (extrafascial)**

The paracervix is transected medial to the ureter but lateral to the cervix. The US and VU ligaments are not transected at a distance from the uterus. Vaginal resection is minimal.

- **Class B1 : transection of paracervix at the ureter**

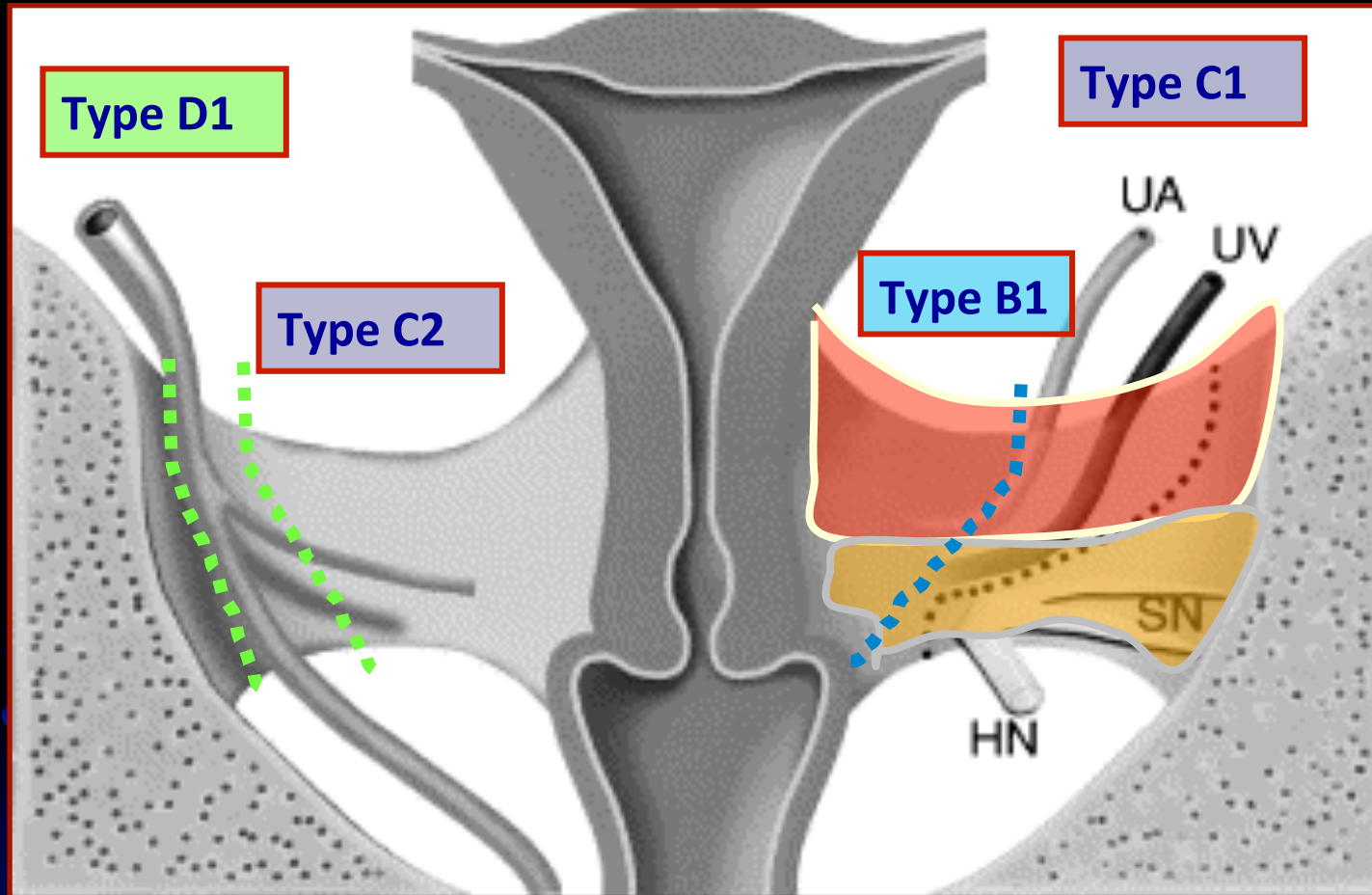
Partial resection of US and VU ligaments. The ureter is unroofed and rolled laterally, permitting transection of the paracervix at the level of the ureteral tunnel. B2: with additional removal of the lateral paracervical lymph nodes.

- **Class C1 : transec. of paracervix at junction with internal iliac**

Transection of US ligament at the rectum and VU ligament at the bladder. The ureter is mobilised completely. 15 to 20 mm of vagina are resected. C1 with nerve preservation. For C2, the paracervix is transected completely, including the part caudal to the deep uterine vein.

- **Class D : laterally extended resection**

D1 is resection along with the hypogastric vessels. D2 plus resection of the adjacent fascial or muscular structures. This resection corresponds to the LEER procedure.

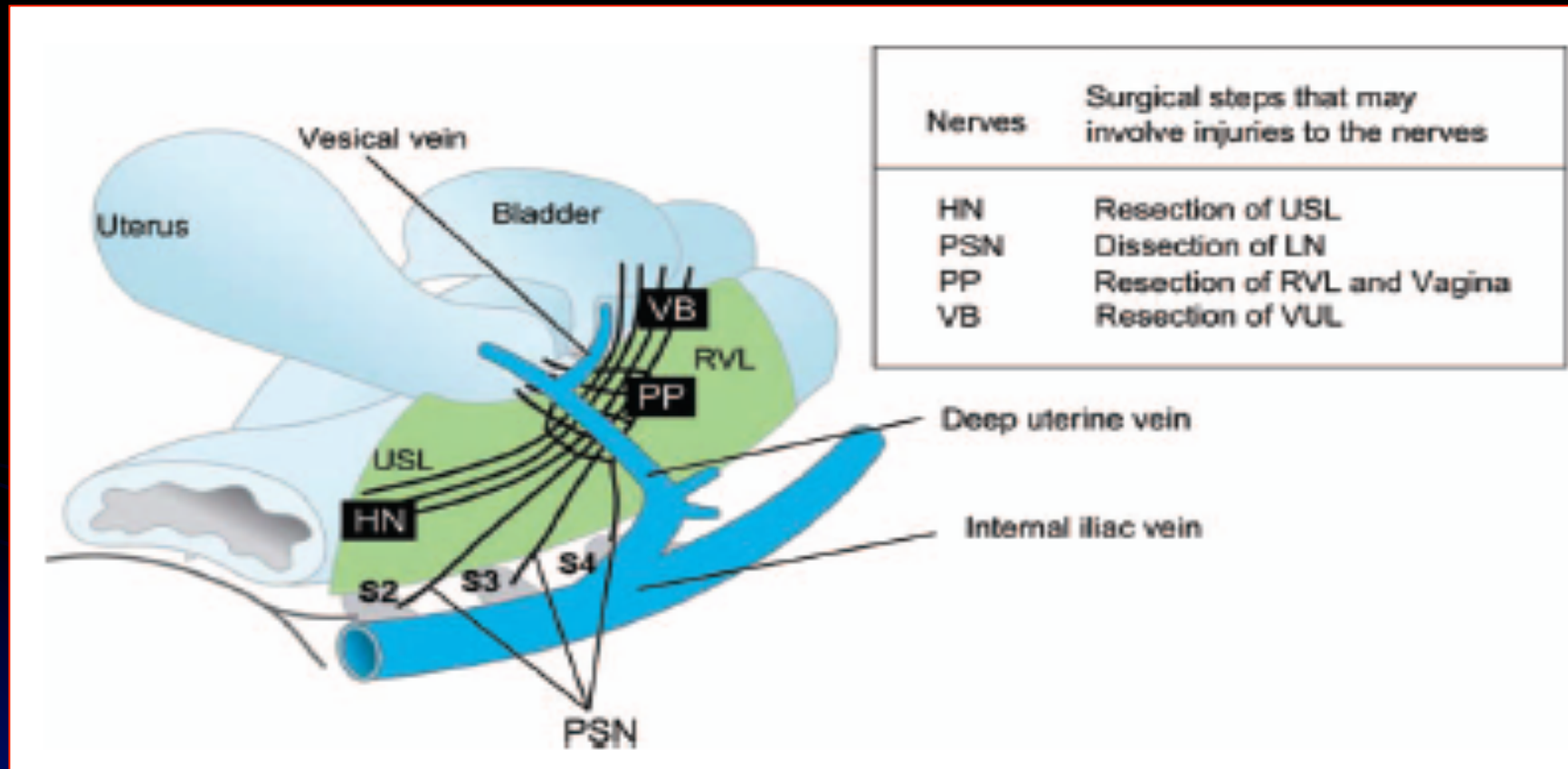


— Vascular part
— Neural part

■ ■ ■ ■ Resection lines
■ ■ ■ ■

A systematic nerve-sparing radical hysterectomy technique in invasive cervical cancer for preserving postsurgical bladder function

N. SAKURAGI*, Y. TODO*, M. KUDO*, R. YAMAMOTO* & T. SATO†



Specific surgical steps to spare the nerves

PARACERVIX (LATERAL PARAMETRIUM)

Deep uterine vein as landmark for paracervix resection and guide to the identification of inferior vesical vein

"VESSEL BY VESSEL"

Uterine artery

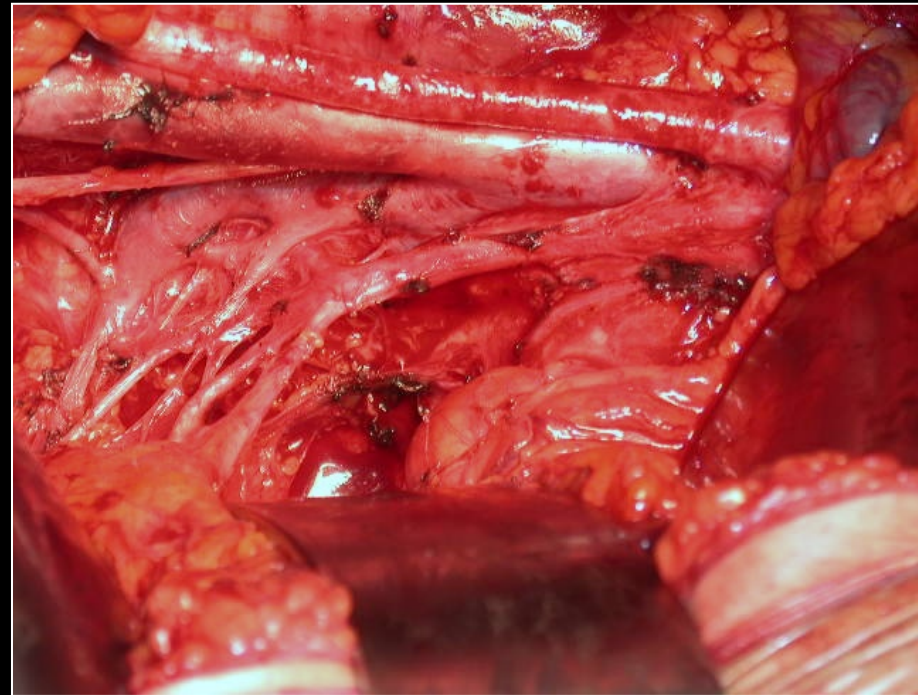
Superficial uterine vein

Deep uterine vein

- Middle rectal artery

Vaginal vein

Vaginal artery



Precise anatomy of the vesico-uterine ligament for radical hysterectomy

Shingo Fujii*, Kenji Takakura, Noriomi Matsumura, Toshihiro Higuchi, Shigeo Yura,
Masaki Mandai, Tsukasa Baba

The posterior leaf of the

VUL is the tissue residing under the ureter connecting the posterior wall of the bladder and the lateral cervix/upper lateral vagina. In the connective tissues, we identified the middle and inferior vesical veins connecting with the deep uterine vein. The division of these veins could separate the urinary bladder with ureters completely from the lateral cervix and upper vagina. The mean blood loss during the separation of the VUL was 20 ± 10 g ($N=59$) and after radical hysterectomy was 189 ± 91.6 g ($N=59$).

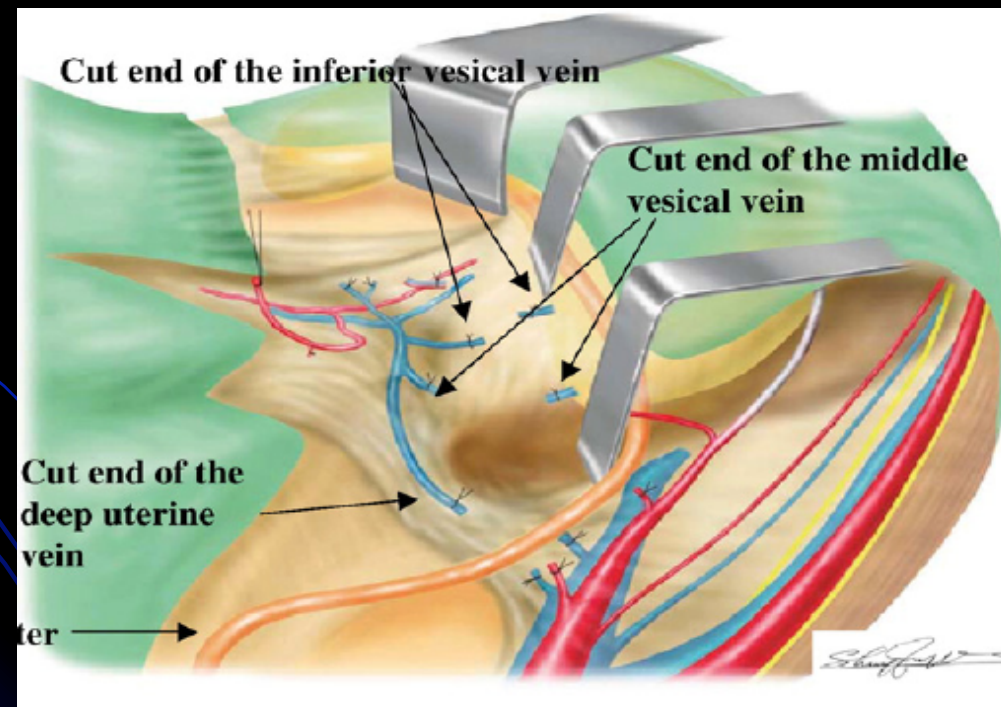
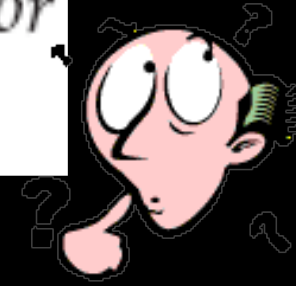


Illustration of the division of the inferior vesical vein which drains into the deep uterine vein.

Step 3: Preserving the distal part of the inferior hypogastric plexus



Vesicouterine ligament contains abundant autonomic nerve ganglion cells: the distribution in histology concerning nerve-sparing radical hysterectomy

A. KATAHIRA*, H. NIIKURA*, K. ITO*, T. TAKANO*, S. NAGASE*, G. MURAKAMI† & N. YAEGASHI*

(Table 1). The interindividual variability was greatest on the dorsal side of the vesical veins with the cell

Dissection of the medial nerve component may be an effective means of sparing pelvic autonomic innervation in some cases of nerve-sparing radical hysterectomy. This technique does, however, have some limitations. We did find differences in the connective intensity (tight or loose) between ganglions and veins. In cases with tight connections, separation was difficult and the ganglions may have been injured. The effect on ganglion function, however, was not assessed. Additionally, it may be difficult to spare nerve function without compromising operative radicality.

Identification and Preservation of the Motoric Innervation of the Bladder in Radical Hysterectomy Type III

Marc Possover, M.D., Steffi Stöber, M.D., Karin Plaul, M.D., and Achim Schneider, M.D., M.P.H.¹

remain intact. The resected vaginal cuff should involve not more than one-third of the vagina to guarantee preservation of the parasympathetic fibers in the recto- and vesicovaginal ligaments.

Tailoring in cervical cancer surgery: adaptation of radicality to tumour spread

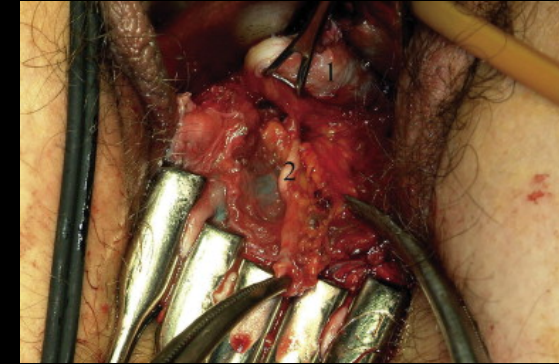
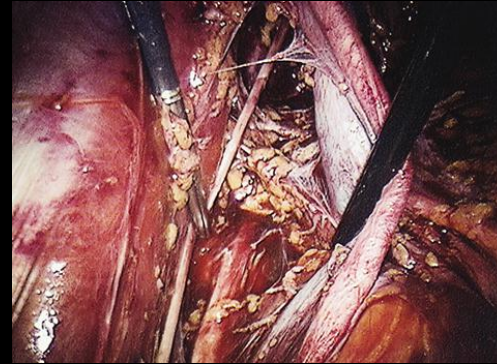
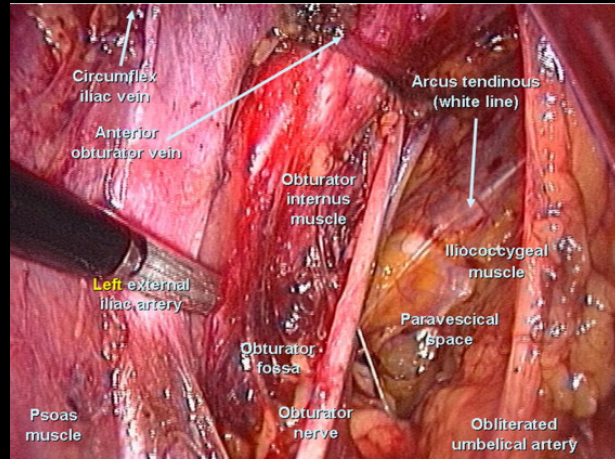
Reducing
radicality

Technical
changes

Advancement
of technology

Chirurgia radicale

- Laparotomica
- Laparoscopica
- Laparoscopica
roboticamente assistita
- Vaginale



- First total laparoscopic RH with pelvic and aortic LND by Nezhat in June 1989
- In the last two decades minimally invasive surgery has become an acceptable alternative
- First robotic RH by Sert and Abeler in 2006

Laparoscopic, robotic and open method of radical hysterectomy for cervical cancer: A systematic review



Puliyath Geetha, M Krishnan Nair¹

Department of Obstetrics and Gynaecology, SUT Academy of Medical Sciences, Post Vencode, Vattappara, Trivandrum,
¹Department of Oncology, SUT Royal Hospital, Pattom Palace, Pattom, Trivandrum, Kerala, India

Address for correspondence: Dr. Puliyath Geetha, Department of Obstetrics and Gynaecology, SUT Academy of Medical Sciences, Post Vencode, Vattappara, Trivandrum-695 028, Kerala, India. E-mail: pgeetha98@yahoo.co.in


Journal of Minimal Access Surgery | July-September 2012 | Volume 8 | Issue 3

- Benefits of MIS are:
 - less wound related problems and morbidity, increases patient comfort, short recovery time, early recovery
 - better visualization, less blood loss
- Robotic surgery better:
 - Faster performance time, increased accuracy, reduced number of errors when compared to conventional laparoscopic surgery
- HOWEVER, debate exists on **ONCOLOGICAL OUTCOME** and **SAFETY**



For example, lymph node metastases were rare when the DaVinci surgical system was used (mean 2%). This contrasts to the traditional surgery where lymph node metastasis rate was 12%. Similarly, tumour was found occasionally at the margin of a robotic or laparoscopic case (mean of 1.7%) but apparently occurred more than three times more commonly in open surgery (mean was 5.5%). One explanation chance is if the difficult cases were done using familiar open methods and easy early-cancer cases were selected for the novel new "toy".

However, because of the inherent biases relating to case selection for different surgical techniques treating the same disease, the only way to reliably look at differences between the individual techniques would be to perform randomised studies comparing the different techniques. Only studies of this type will lead to potentially valid conclusions about key oncological outcomes, quality of life and risks of major morbidity.



Linfoadenectomia

Survival by site positive nodes

Author (year of publication)	Study cohort	Index of survival	Survival by lymph node metastasis (%)			
			No metastasis	Pelvic node	Common iliac node	Paraortic node
Garipagaoglu et al. (1999) ⁶⁰	Ib-IIa	5-year OS	94.7	65.4	NA	NA
Lai et al. (1999) ⁶¹	Ib-IIb	5-year OS	87.3	68.2	NA	NA
Morice et al. (1999) ¹¹	Ib-IIb	3-year OS	94	64	(Included in the pelvic node)	35
Kim et al. (2000) ¹³	Ib-IIa	5-year OS	95	84.6	(Common iliac and/or paraortic node) 20	
Aoki et al. (2000) ⁶²	Ib-IIb	5-year DSS	NA	NA	38.9	NA
Takeda et al. (2002) ⁶²	Ib-IIb	5-year DSS	92.5	80.3	46.3	33.3

OS, overall survival; DSS, disease-specific survival; NA, not available

PROGNOSTIC SIGNIFICANCE OF NODES METASTASIS

Sakuragi et al. 2007

For node negative patients there was a correlation between extent of lymphadenectomy and cancer-specific survival

>30 nodes: 36% less like to die than <10 nodes

Table 4. Five-Year Survival Among Node Negative Patients Stratified by Stage and Number of Lymph Nodes Removed

	≤10 Nodes		11-20 Nodes		21-30 Nodes		>30 Nodes	
	No. (%)	95% CI	No. (%)	95% CI	No. (%)	95% CI	No. (%)	95% CI
IA2	124 (94)	88-97	263 (99)	96-100	159 (98)	94-99	93 (99)	92-100
IB	603 (89)	86-92	1383 (90)	88-92	1042 (90)	88-92	792 (93)	91-95
IIA	35 (79)	58-90%	63 (85)	71-93	50 (85)	70-93	41 (80)	63-90

CI indicates confidence interval.

HR= 0,64;95% CI, 0.43-0,96

Shah. M. et al, Cancer, 2010

Node metastasis

Governor of survival:

the removal of all affected nodes to extirpate all tumor cells

Indicator of survival:

the removal of affected nodes not improve survival and complete lymphadenectomy is unnecessary

The truth probably lies in between

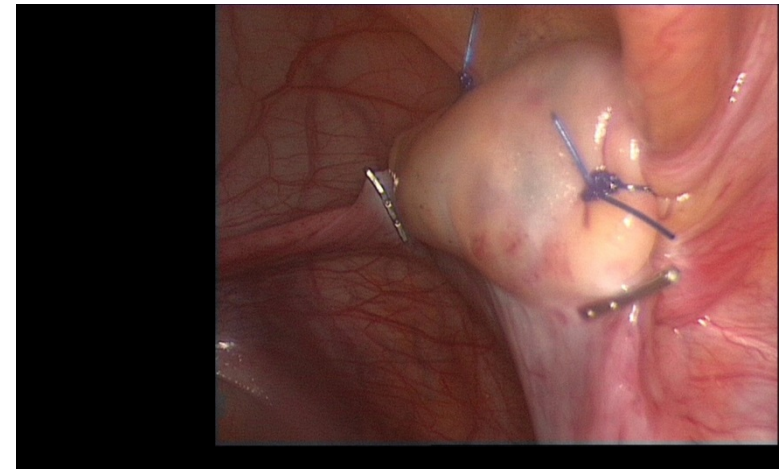


Ovariectomy

Ovarian metastases in early-stage cervical cancer (IA2–IIA): a multicenter retrospective study of 1965 patients (a Cooperative Task Force study)

F. LANDONI*, V. ZANAGNOLO*, L. LOVATO-DIAZ*, A. MANEO†, R. ROSSI†, A. GADDUCCI‡, S. COSIO‡, T. MAGGINO§, E. SARTORI||, C. TISI§, P. ZOLA¶, F. MAROCCO¶, E. BOTTERI# & K. RAVANELLI*

*Department of Gynecology Oncology, European Institute of Oncology (EIO), Milan, Italy; †Department of Obstetrics/Gynecology, University of Milan (Bicocca), Milan, Italy; ‡Department of Obstetrics/Gynecology, University of Pisa, Pisa, Italy; §Department of Obstetrics/Gynecology, University of Padova, Padova, Italy; ||Department of Obstetrics/Gynecology, University of Brescia, Brescia, Italy; ¶Department of Obstetrics/Gynecology, University of Torino, Torino, Italy; and #Division of Epidemiology, European Institute of Oncology (EIO), Milan, Italy



suggestion for the criteria to be met could be the following: age 45 or younger, no macroscopic abnormalities at the inspection of the ovaries, FIGO stage IA1–IIA (<4 cm), squamous histology, and greater than 3 mm of unaffected peripheral stromal thickness; even though still debatable, the last risk factor can be preoperatively assessed by magnetic resonance imaging with relatively high predictive value.

Table 4. Stage distribution, histologic type, and incidence of ovarian metastases in early-stage cervical cancer (series from the literature)

Authors (reference)	Patients	FIGO stage	Ovarian metastases squamous carcinoma (%)	Ovarian metastases adenocarcinoma (%)	P
Sutton ⁽⁶⁾	990	IB	4/770 (0.5)	2/121 (1.7)	0.19
Natsume ⁽¹⁰⁾	82	IB–IIA	9/82 (10.9)		
Yamamoto ⁽¹¹⁾	631	IB–IIIB	2/485 (0.4)	12/146 (8.2)	NA
Nakanishi ⁽⁸⁾	1304	IA2–IIB	14/1064 (1.3)	15/240 (6.3)	NA
Present study	1965	IA2–IIA	7/1284 (0.5)	9/380 (2.4)	0.0014 ^a

^aP values obtained by Chi-square test or Fisher exact test.

Ovarian metastase in cervical cancer multivariate analisys

<u>parameter</u>	<u>odds ratio</u>	<u>95% CL</u>	<u>p</u>
FIGO stage	5.981	1.50 – 23.8	.011
Histology (adeno)	8.224	2.39 – 28.2	<.001 *
Stroma unafect. <3mm	9.443	1.14 – 77.8	.037

Guidelines to preserve the ovaries in R.S.

- Women 40 years old or younger
- No morphological abnormality in the ovary
- Stage FIGO IA₂ - IB₁ - IIA
- Squamous, >3mm uninvolved tissue, LVSI -
- No hystory of breast cancer
- No risk of familial ovarian cancer

Talk Plan

- **Epidemiologia**
- **Prevenzione e lesioni precancerose**
- Strategie nel cancro negli stadi iniziali:
 - Chirurgia radicale
 - Complicanze
 - Trattamento conservativo
 - Trattamento adiuvante
- **Strategie nel cancro localmente avanzato**
- **Futuro**

- Cervical cancer accounts for 6% of all cancer in women (3700 new cases/year in Italy)
- Standard treatment of early stage cervical cancer has been either radiotherapy or radical hysterectomy with pelvic node dissection (**level 1**)
- As an increasing number of early cervical cancer are diagnosed in **young women**, a less radical approach aiming at preserving fertility potential is becoming crucial

From 2003-2007, the median age at diagnosis for cancer of the cervix uteri was 48 years of age

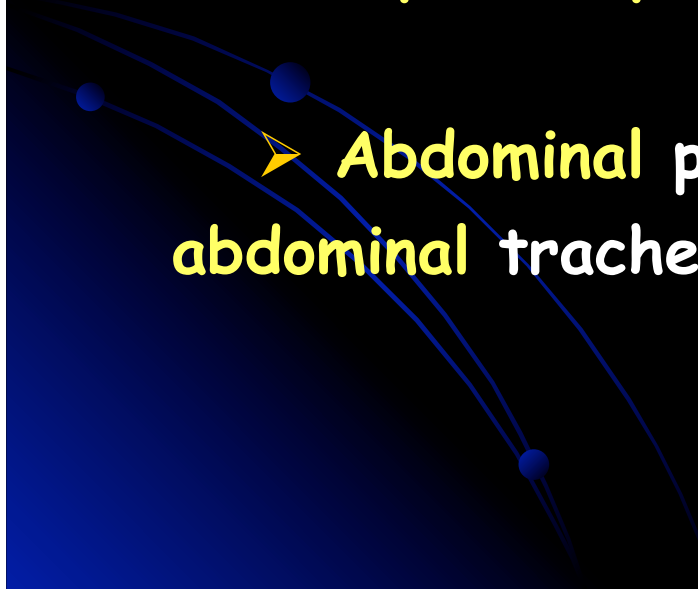
Approximately 0.2% were diagnosed under age 20;

14.5% between 20 and 34;

26.1% between 35 and 44;

SEER Data

Fertility-Sparing Surgery in early stage CC

- **Laparoscopic** pelvic lymphadenectomy & radical **vaginal** trachelectomy (Dargent et al. -1994)
 - **Laparoscopic** pelvic lymphadenectomy & radical **laparoscopic** trachelectomy (Lee et al. 2003)
 - **Abdominal** pelvic lymphadenectomy & radical **abdominal** trachelectomy (Smith et al.1997-Abu-Rustum 2006)
- 

Laparoscopic pelvic lymphadenectomy & VRT

Reference	Stage	Relapses	SCC	Adeno	Other
Sheperd	IA2-IB1	3/112	ND	ND	ND
Hertel	IA1-IB1	4/108	1/75	3/33	--
Mathevet	IA1-IIA	4/95	3/76	1/19	1/1*
Covens	IA1-IB1	7/93	4/40	3/50	--
Plante	IB1	3/72	1/42	1/30	1/1*
Sonoda	IA1-IB1	1/36	ND	ND	ND
Burnett	IB1	0/19	--	--	--
Schlaert	IA2-IB1	0/10	--	--	--

* excluded



TOTAL 22/545 (4%)

Laparoscopic pelvic lymphadenectomy & VRT

	Relapses	
	< 2 cm	> 2 cm
Sheperd	ND	ND
Hertel	3/107	1/1
Mathevet	0/74	4/21
Covens	6/85	1/8
Plante	0/64	2/8
Sonoda	ND	ND
Burnett	ND	ND
Schlaert	ND	ND
TOTAL	9/330 2.7%	8/38 21%

RVT - Obstetric outcomes

- **Pregnancy rates of 41-79%**
- 208 reported pregnancies, which resulted in 134 (64%) third trimester live births
 - The rate of first trimester miscarriage was 18%
 - The rate of second trimester miscarriage was 10%
 - The rate of preterm delivery (< 37 weeks) was 20%
- **Term delivery was reached in 38% of all pregnancies**

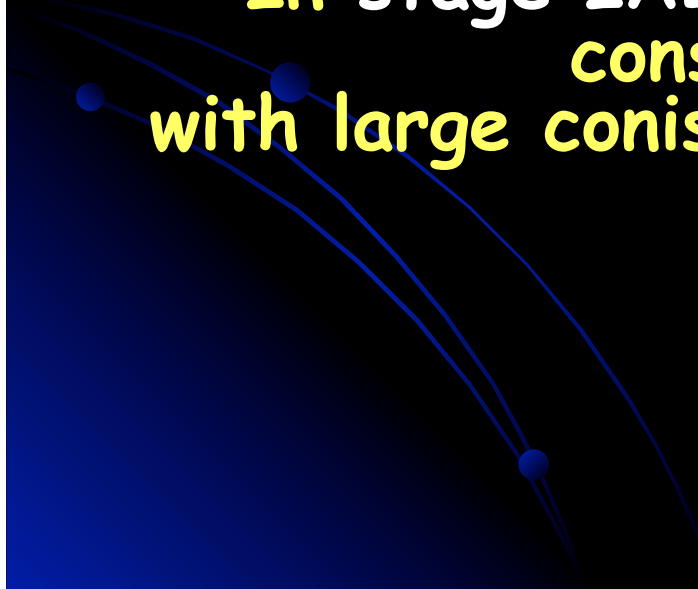
RVT - KEY POINTS

- Safe and feasible procedure to perform in early-stage small volume cervical cancers.
- The tumor recurrence rate is 4% and the mortality rate is about 3%. These results are comparable to those observed after radical surgery.
- **Lesion size > 2cm is probably the most important risk factor for recurrence.**
- Increased incidence of late miscarriages and preterm deliveries.
- Term delivery is reached in 38% of all pregnancies.

Take home message !

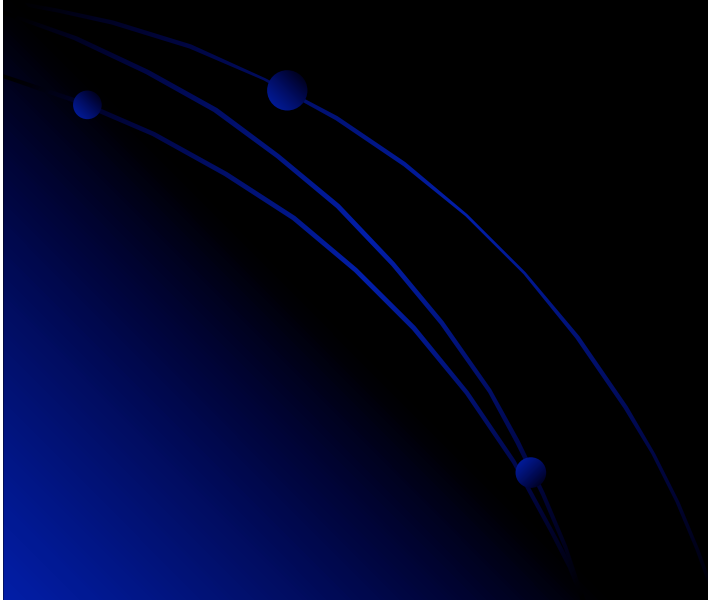
The operation has an acceptable complication profile but is associated with a *significant incidence of miscarriage and premature labour.*

In stage IA2 should be offered a more conservative approach with large conisation & pelvic node dissection.



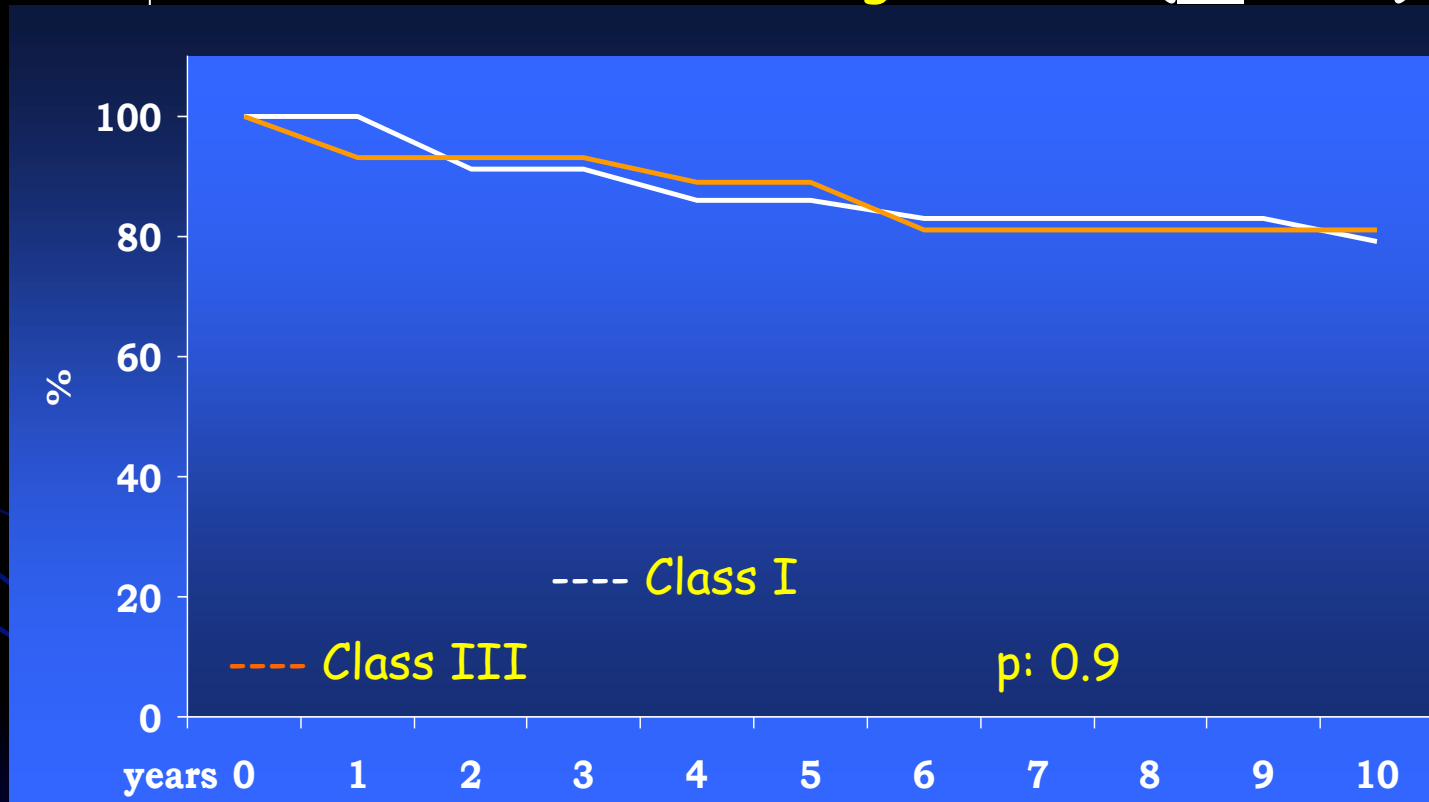
OPEN QUESTION

In stage Ib1 cervical cancer is the removal of parametria always necessary ?



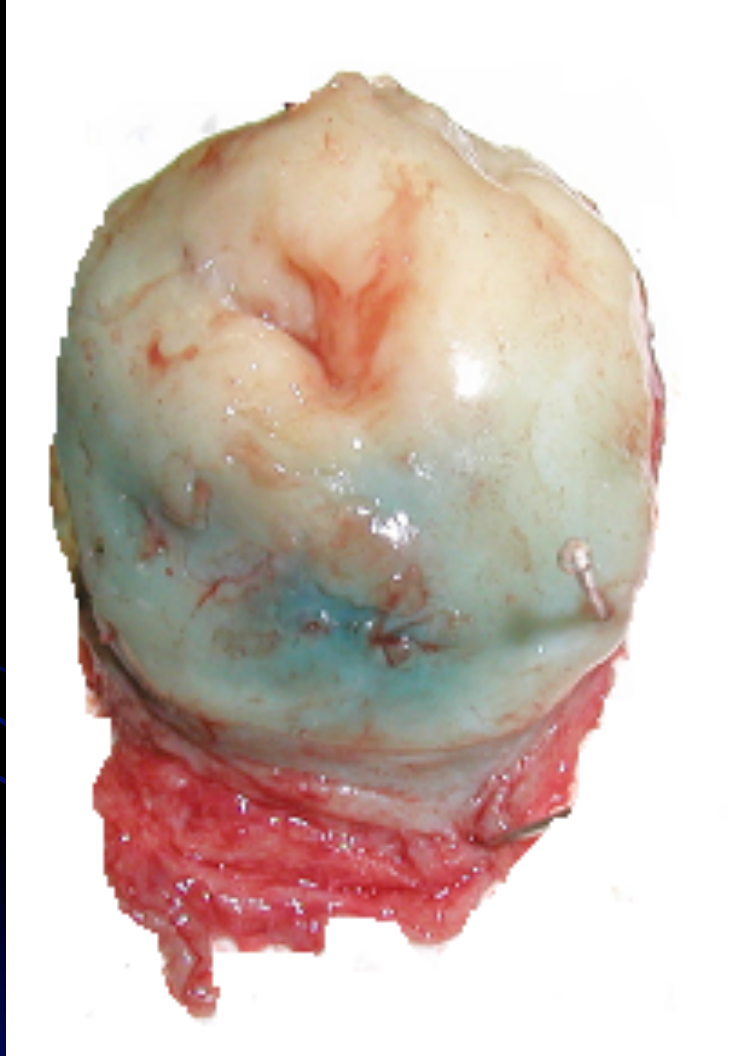
Cervical Cancer Surgery (1982-1986)

Class I vs Class III in stage IB1 CC (< 3 cm)



Fertility-sparing procedure in CC

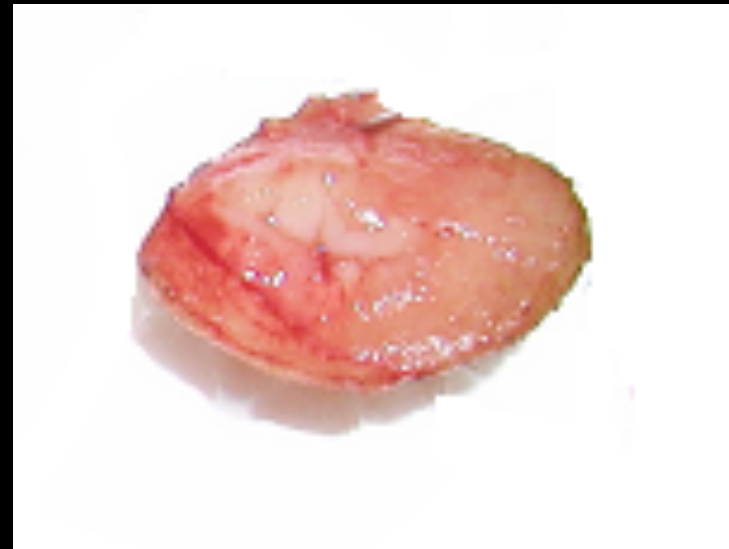
- SLNM, +/- NACTH, laparoscopic pelvic lymphadenectomy & simple trachelectomy or large cone (Rob et al. 2003)
- NACTH + pelvic lymphadenectomy + deep cone (Maneo et al. 2004)
- NACTH + pelvic lymphadenectomy + deep cone (case reports)
- Chemo-surgical treatment (IEO experience)



Simple
trachelectomy



Cone



IEO Experience



- Tumor diameter ≤ 2 cm
- Laparoscopically pelvic LA & cervical cone
- F-UP if no evidence of risk factors

□ Tumor diameter $> 2 \leq 3$ cm

- Laparoscopically pelvic LA

NEGATIVE NODES

- Platinum&taxol-based chemotherapy for 3 cycles
- Simple trachelectomy/Cervical cone

PRO

- These data demonstrate that simple trachelectomy / cervical cone can be safely performed.
- Data *are comparable* with more radical procedure
- Pregnancies rate is slightly better than RVT

CONS

- Low compliance to conservative program (< 40% in all)
- Chemo-cone: alopecia
- Chemo-cone: identify endocervical involvement, to isthmic surveillance (IUO preserved)
- *Chemo-cone: theoretical teratogenicity*

Taking home message

Modified-less radical surgical treatment

Less radical local surgical treatment of early **vulvar** cancer with negative SLNM is accepted

Less radical local surgical treatment of early **breast** cancer with SLNM is accepted

Less radical local surgical treatment of early **CC** with negative Nodes /SLNM is acceptable?

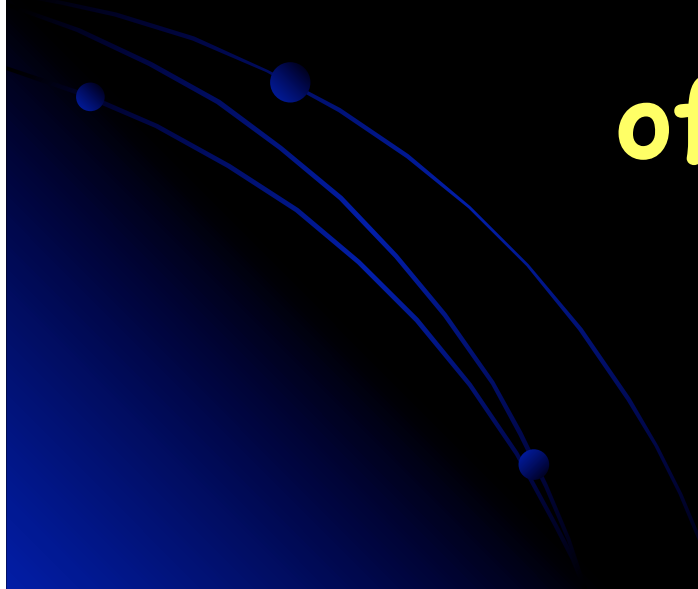


Talk Plan

- **Epidemiologia**
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 - **Trattamento adiuvante**
- **Strategie nel cancro localmente avanzato**
- **Futuro**

Clinical scenarium
beyond surgery

Adjuvant treatment
of early stage



When is RT or Chemo/RT Indicated After Radical Hysterectomy?

Radiation if two of the following:

- **deep invasion, large tumor or vascular invasion**
 - GOG 92 (Sedlis A et. al .A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study. Gyn Onc 73:177-183, 1999)

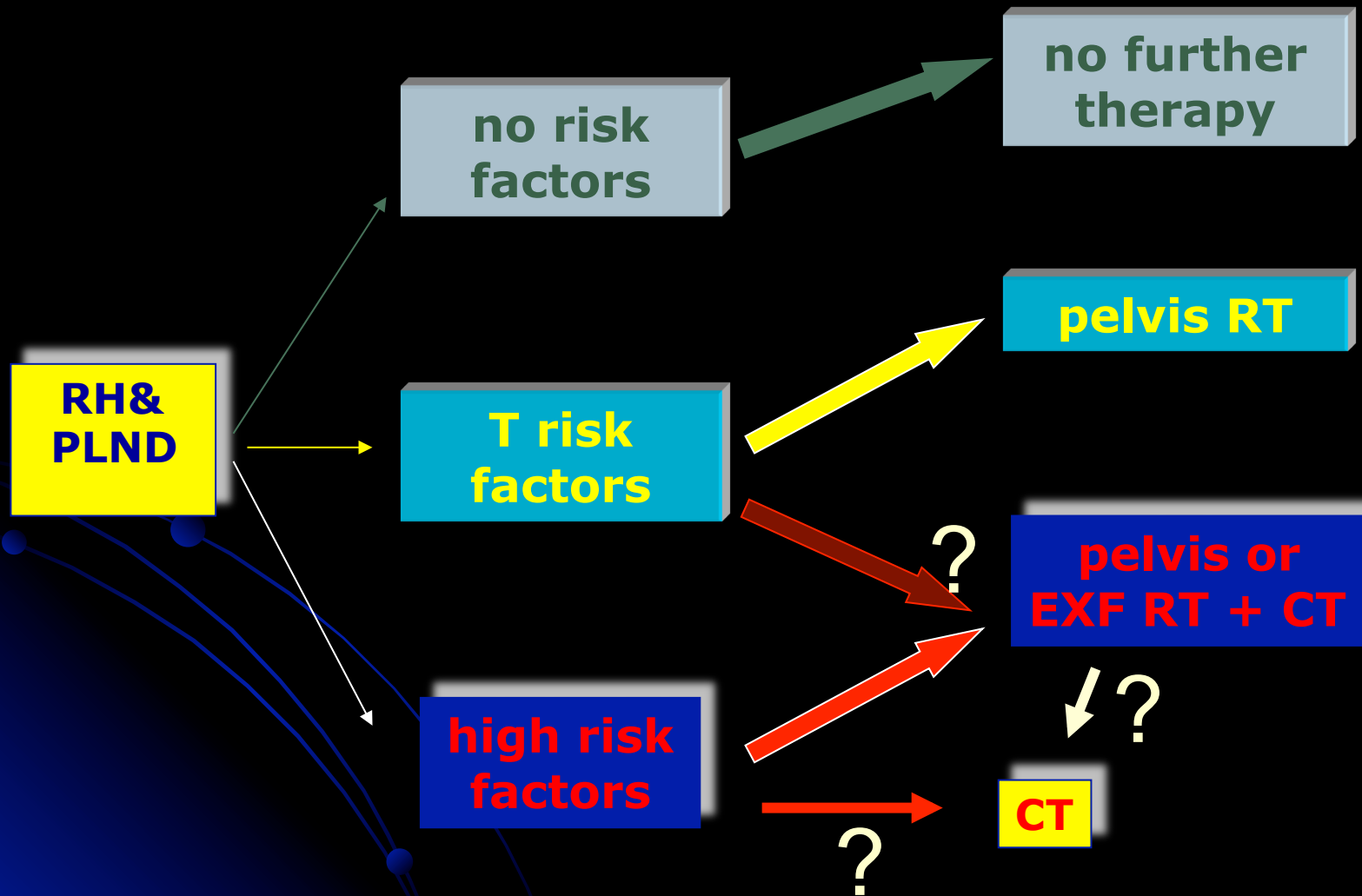
Chemo-RT if one of the following:

- **Positive margin, parametrial extension, positive node**
 - GOG 109 (Peters WA et. al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol 18:1606-1613, 2000)

Which treatment ?

- Radiotherapy
 - Chemotherapy
 - Chemo-radiation
- 

Adjuvant RT after RH & PLND





**OSPEDALE
CANNIZZARO**

U.O. di Ostetricia e Ginecologia

Direttore: Prof. Paolo Scollo

**Centro di Riferimento Regionale
per l'Oncologia Ginecologica**

GURS n. 53 del 14/12/2012



**OSPEDALE
CANNIZZARO** CATANIA

AZIENDA OSPEDALIERA PER L'EMERGENZA

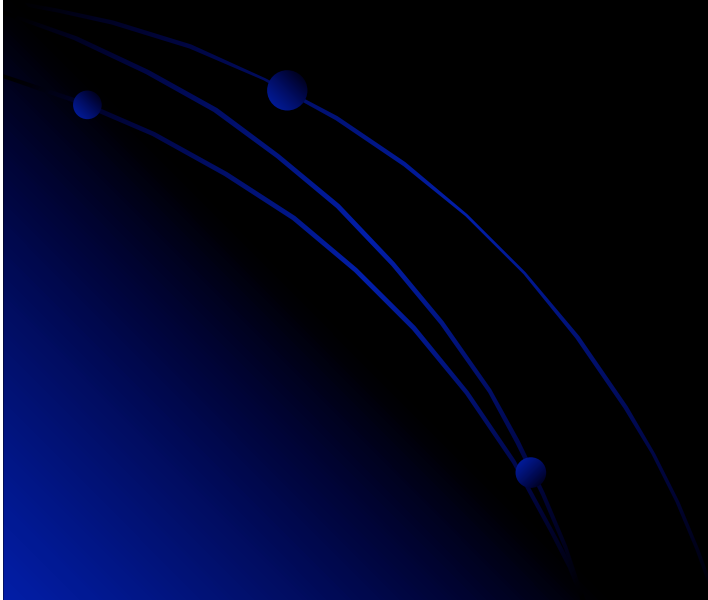
(ANNI 2000-2012)

Stadio FIGO	N°
IA/IB	108
IIA/IIB	186
IIIA/IIIB	26
IVA/IVB	15
sconosciuto	11
Totale	346

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- **Futuro**

Issue of the next
AIRO congress ?



Carcinoma invasivo
(Stadio FIGO I B2 (> 4 cm) e stadi superiori)

1. Chemioterapia neoadiuvante e successiva chirurgia radicale.

2. Chemio-radioterapia esclusiva.

3. Chemio-radioterapia neoadiuvante ??



**NEOADJUVANT TIP
(PACLITAXEL, IFOSFAMIDE, AND CISPLATIN) CHEMOTHERAPY
FOLLOWED BY RADICAL SURGERY IN PATIENTS WITH
LOCALLY ADVANCED SQUAMOUS CELL CERVICAL CARCINOMA:
A MONOCENTRIC EXPERIENCE ON 136 PATIENTS
(JULY, 1997 - NOVEMBER 2010)**

PAOLO SCOLLO

**DEPARTMENT OF OBSTETRICS AND GYNECOLOGY
CANNIZZARO HOSPITAL - CATANIA - ITALY**



Talk Plan

- **Epidemiologia**
- **Prevenzione e lesioni precancerose**
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 - Trattamento conservativo
 - Trattamento adiuvante
- **Strategie nel cancro localmente avanzato**
- **Futuro**

Take home message

- Migliorare strategie di prevenzione primaria e screening= non ammalare !!
- **Ruolo della chemioterapia e nuovi farmaci.**
- Maggiore ricerca sulla biologia della malattia.
- **Trattamenti conservativi nella malattia invasiva.**
- **Attesa di conclusione degli studi clinici.**
 - strategia NACT+surgery vs CHT-RT
 - chirurgia mininvasiva vs laparotomica
- **Chirurgia nerve-sparing (much mature data)**
- **Ruolo nuove diagnostiche: PET/TC**

*Cominciate col fare ciò che
è necessario.....*

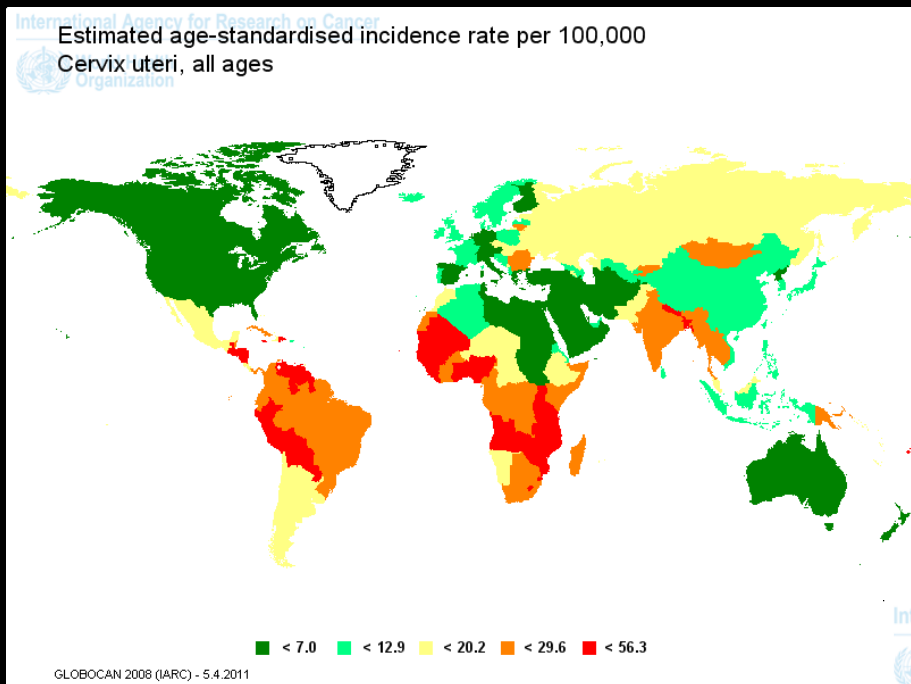
poi ciò che è possibile...

*E all'improvviso vi
sorprenderete a fare
l'impossibile.*

San Francesco d'Assisi

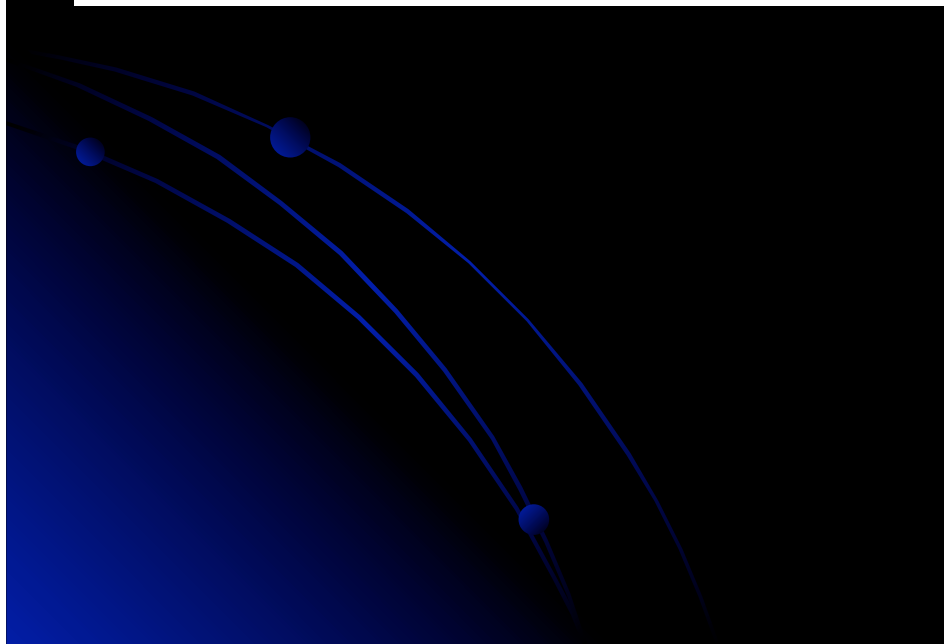
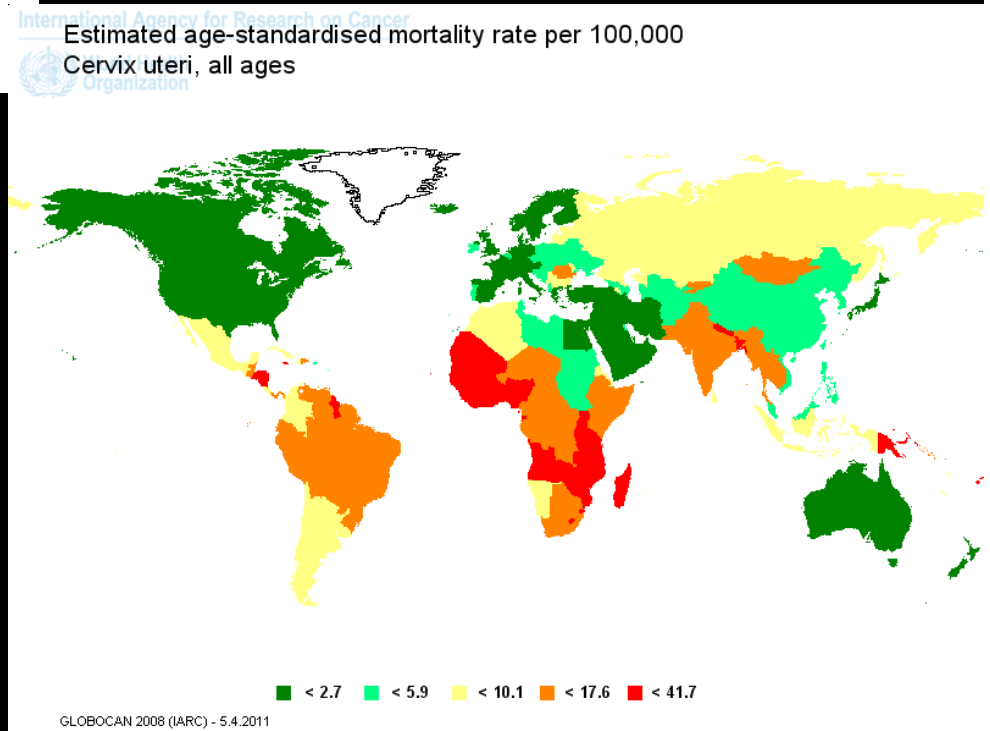


Grazie!



Incident cases in 2008	
Europe	54,517
Worldwide	530,232

Deaths in 2008	
Europe	24,874
Worldwide	275,008





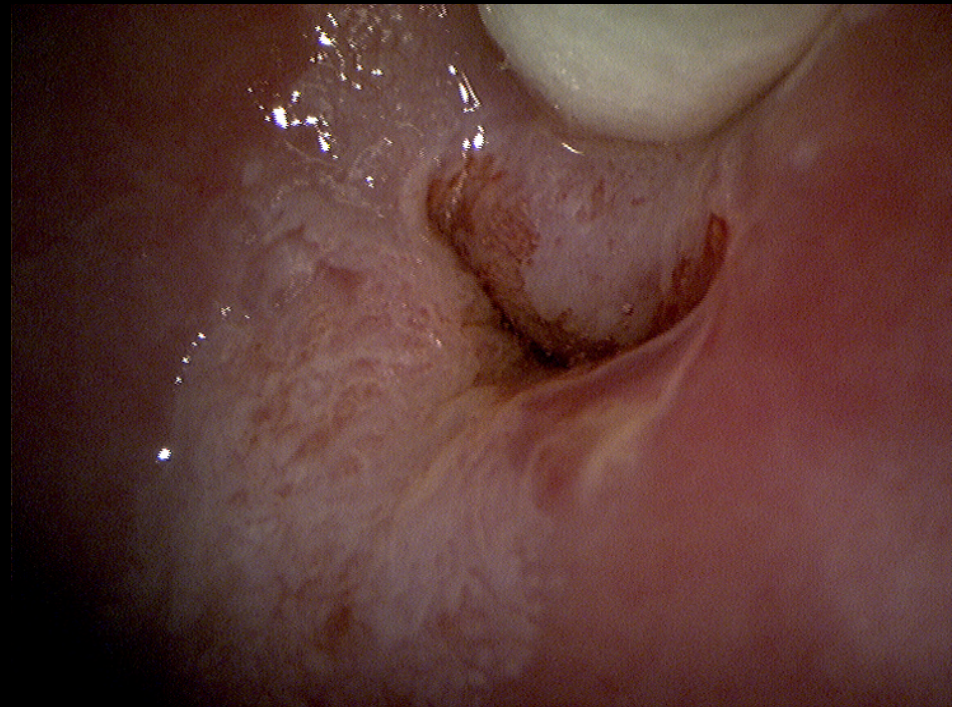
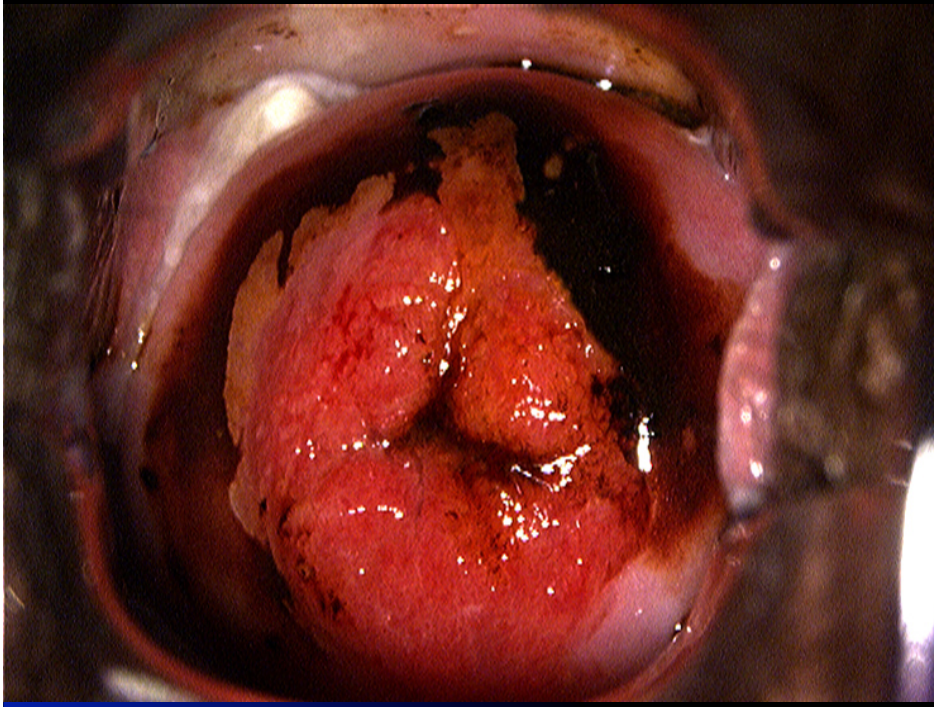
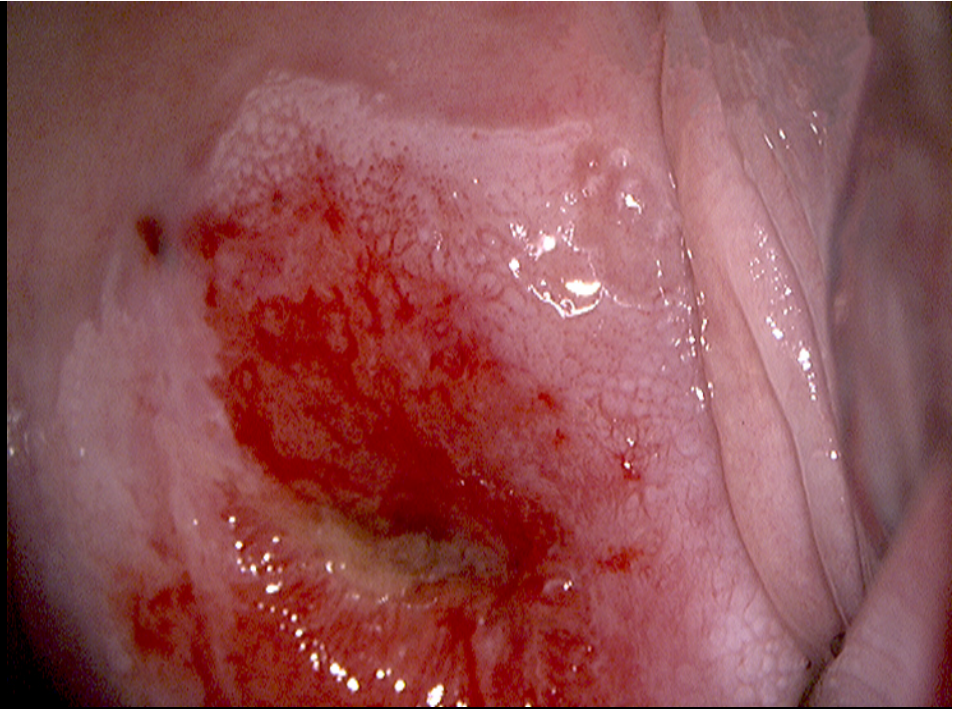
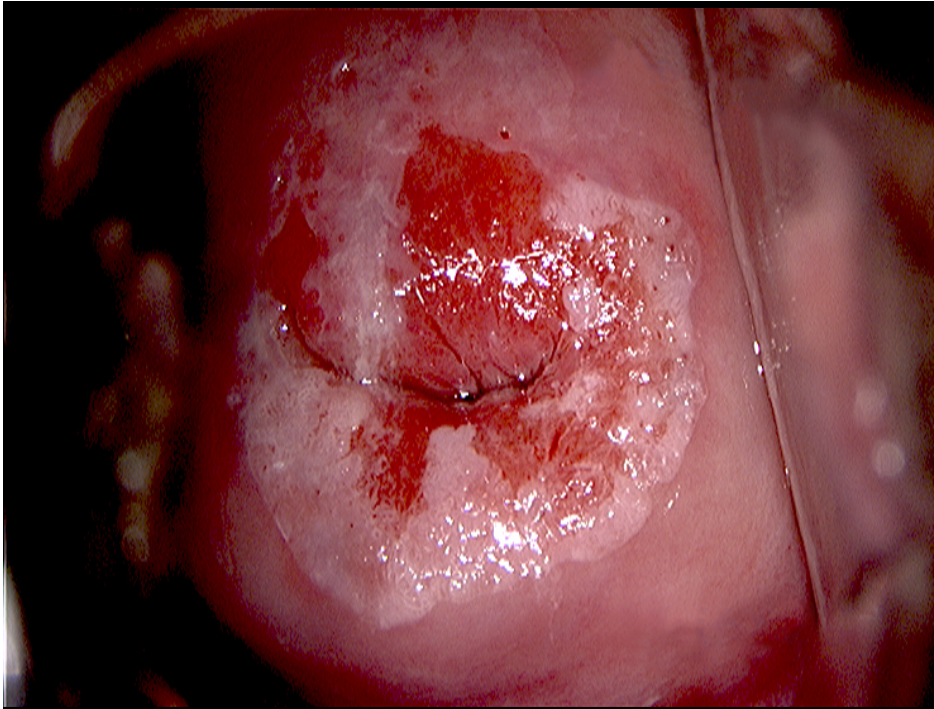
L'obiettivo dello screening del cervicocarcinoma è identificare le lesioni pre-invasive per trattarle in modo da ottenere

Il 100% di sopravvivenza a 5 anni

USA:

Dopo screening si è ottenuta una riduzione dei nuovi casi di neoplasia da 20.000 ogni anno (1960) a 13.000 ogni anno (dal 1991)

In Italia riduzione di incidenza del 40%
Incidenza di 12.3x100.000 donne ogni anno



Obiettivi del management delle precancerosi

Identificare la lesione

Escluderne la invasività

Preservare la fertilità

Utilizzare tecniche "cost-effective"

Utilizzare tecniche a bassa morbilità

E

Ottenere un controllo locale della malattia

Prevenire le lesioni invasive

Management of precancerosis in Europe.

CIN 1

Observation or Treatment

Observation or treatment
if colposcopy is satisfactory.

Treatment with excisional methods
if unsatisfactory colposcopy



Management of precancerosis in Europe.

CIN 2-3 Treatment

Ablative methods is acceptable
if colposcopy is satisfactory.

Excisional methods
if unsatisfactory colposcopy or suspected
glandular lesions.

Take home messages

Molta pubblicità, poca informazione.

Necessità che chi tratta, conosca bene la patologia.

Gestione personalizzata.

Attenzione agli over-treatment soprattutto se ripetuti.

Chirurgia mininvasiva ma non per questo senza potenziali complicanze a volte con compromissione importante della QoL.

Talk Plan

- **Epidemiologia**
- **Prevenzione e lesioni precancerose**
- **Strategie nel cancro negli stadi iniziali:**
 - **Chirurgia radicale**
 - **Complicanze**
 - **Trattamento conservativo**
 - **Trattamento adiuvante**
- **Strategie nel cancro localmente avanzato**
- **Futuro**

Recommendations from FIGO Gyn Onco Committee - 2

- **Stage 0**
 - Delete stage 0
- **Stage IA and IB**
 - No changes recommended
- **Stage IIA**
 - Size has similar effect on prognosis similar to IB (Hong JH et al 2005)
 - Recommended to substage IIA to
 - **IIA₁** : tumour size of less than or equal to 4 cm with involvement of less than upper 2/3 of vagina
 - **IIA₂** : tumour size of more than 4 cm with involvement of less than upper 2/3 of vagina

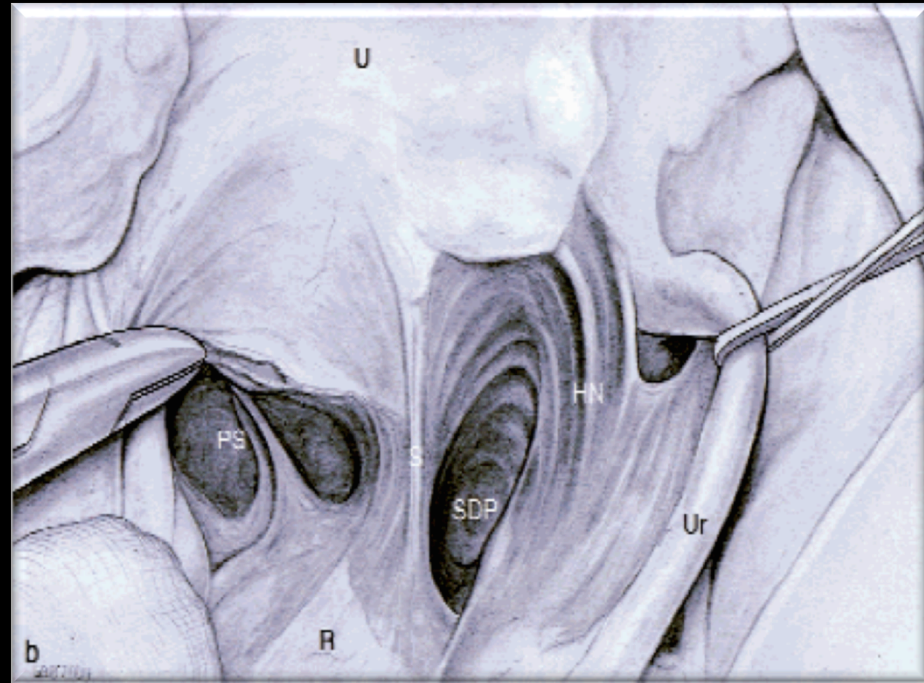
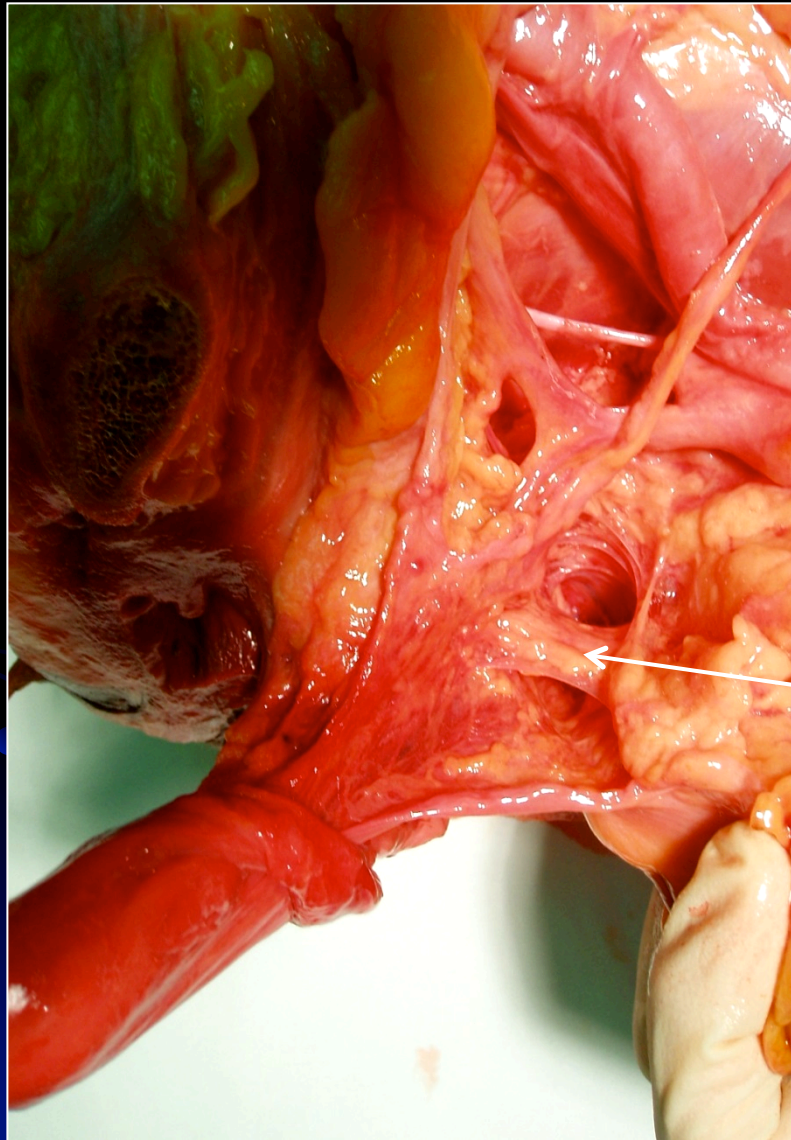
L y m p h n o d e



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.

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.

Compartimento posteriore (--)



The connective tissue bundle that emerges between Okabayashi's and Latzko's spaces is the so-called mesoureter (or Ureterblatt or ureteral leaf²⁵) (Figures 4 and 7). This mesoureter is the one in which 2 visceral pelvic fasciae are fused, and between which the ureter, hypogastric nerve, and ureteral branch of the internal iliac vessels pass

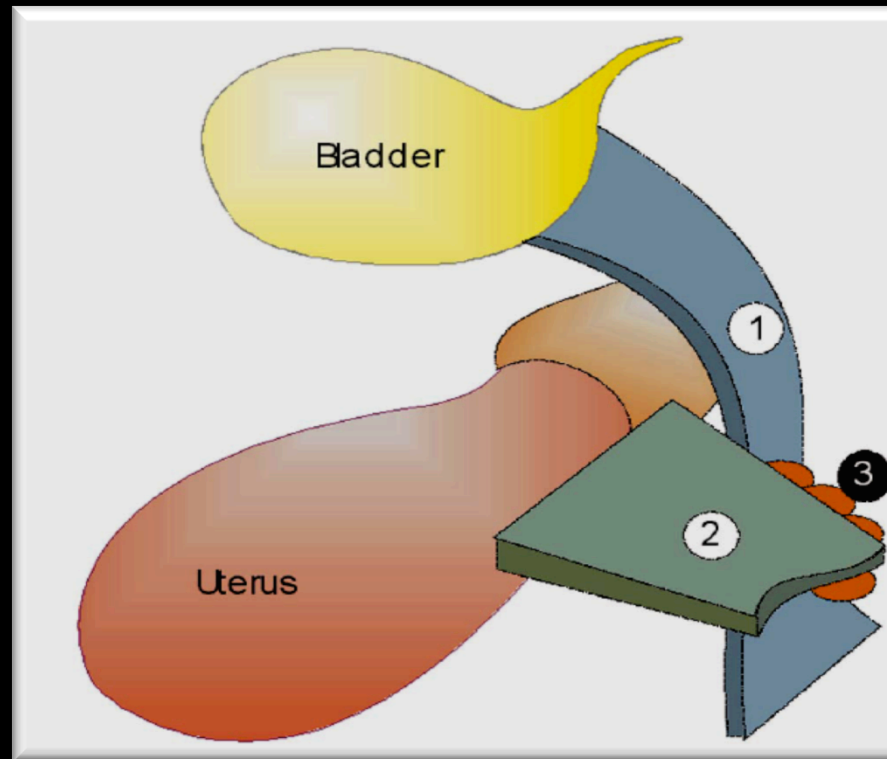
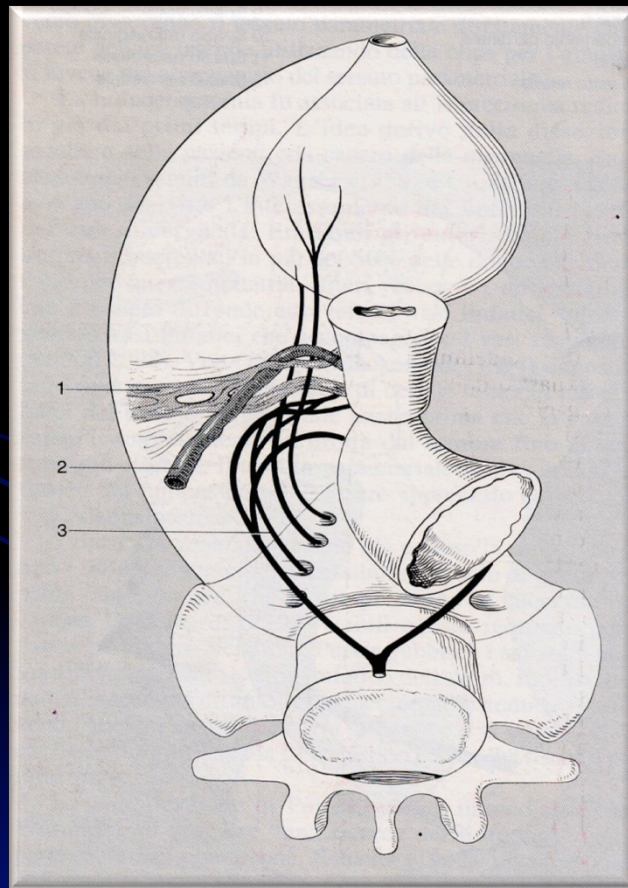
Yoshihiko Yabuki, MD, DMSc,^a

American Journal of Obstetrics and Gynecology (2005) 193, 7-15

Compartimento centrale (+-)

Le strutture nervose (HN e PSN) sono confluenti (a formare IHP) ed identificabili
E' in questa fase indispensabile identificare e risparmiare i PSN quando questi si
fondono con i HN

Importanza di landmarks vascolari (deep uterine vein, middle rectal artery)



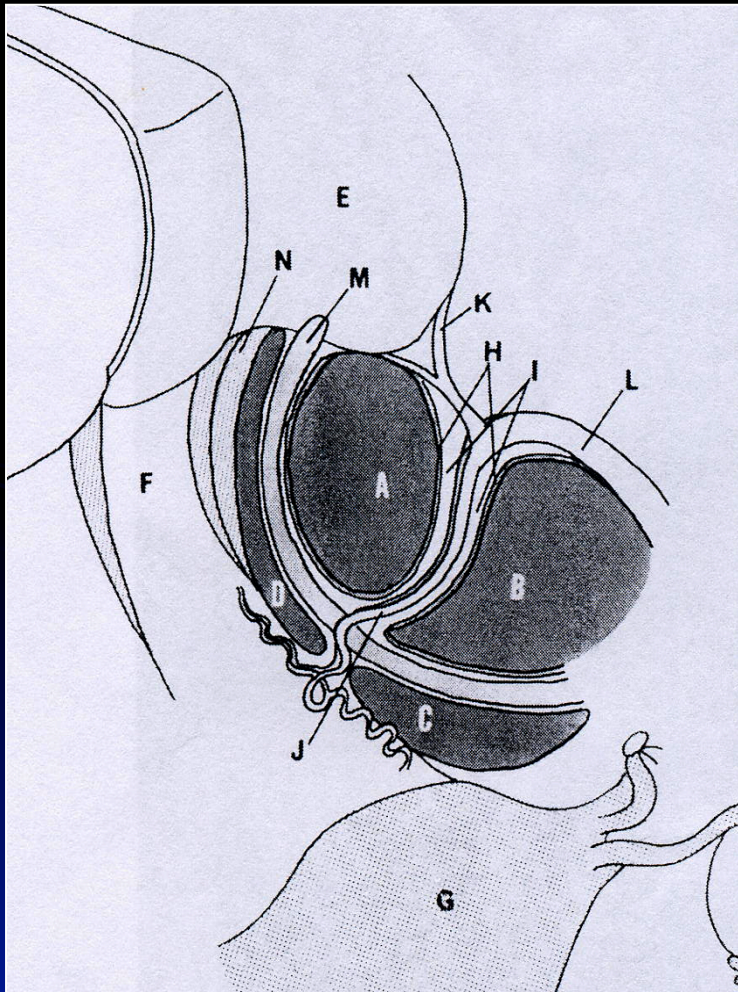
Identification and Preservation of the Motoric Innervation
of the Bladder in Radical Hysterectomy Type III

Marc Possover, M.D., Steffi Stöber, M.D., Karin Plaul, M.D., and Achim Schneider, M.D., M.P.H.¹

Department of Gynecology, Friedrich Schiller University, Bachstrasse 18, 07740 Jena, Germany

Compartimento anteriore (++)

- Le strutture nervose sono fuse in un unico fascio connettivo-vascolo-nervoso: il legamento vescico-uterino (VUL)



The connective tissue bundle that emerges between the paravesical space and Okabayashi's paravaginal space is the deep layer of the vesicouterine ligament advocated by Okabayashi (Figures 3, 6, and 7).^{8,9,20} This deep layer of the vesicouterine ligament was found to be a neurovascular bundle that connected the bladder and the lateral ligament of the pelvis.^{14,15}

The deep, posterior leaf of VUL is a well known structure developed during radical hysterectomy that contains vesical veins draining into the deep uterine vein. Thus the deep layer probably contains detrusor nerve fibers and ganglions originating from the PSN and going toward the bladder neck.

Therefore, adequate treatment of the VUL deep layer may become the most critical step of any NSRH.

Resection of the embryologically defined uterovaginal (Müllerian) compartment and pelvic control in patients with cervical cancer: a prospective analysis

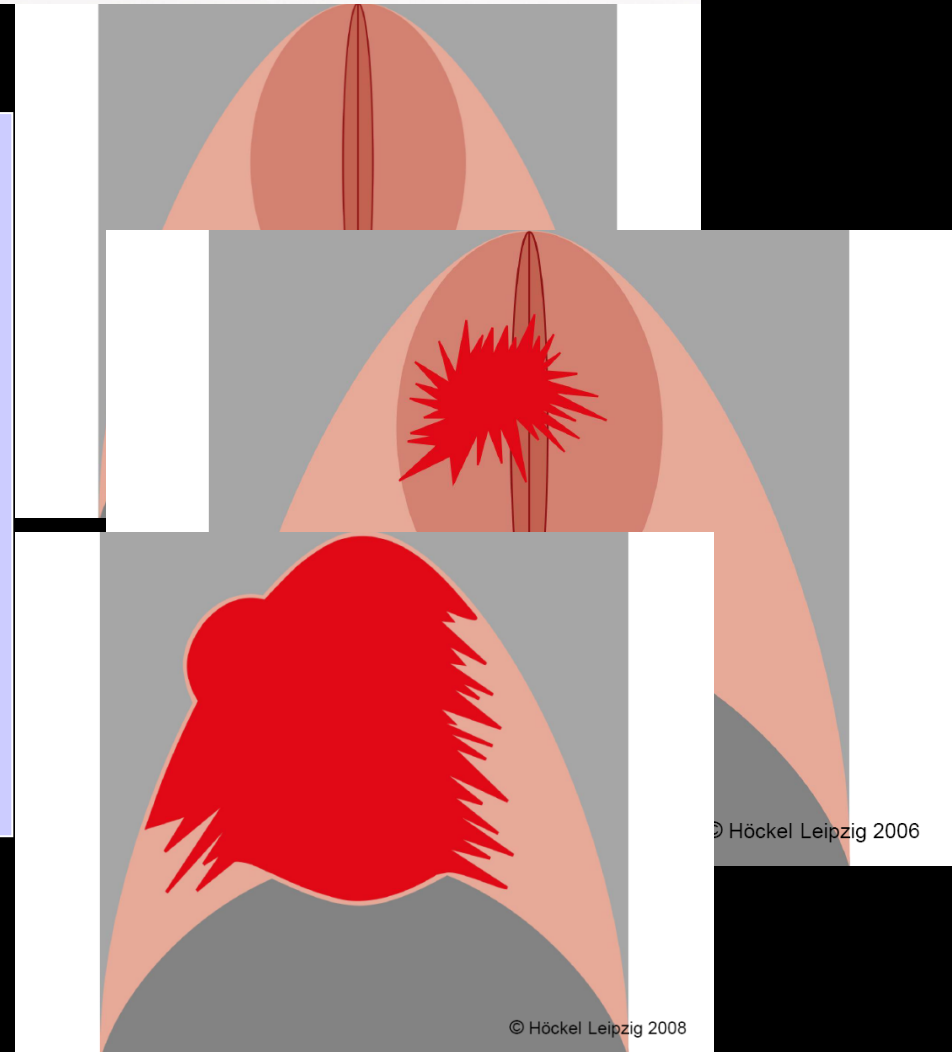


Michael Höckel, Lars-Christian Horn, Norma Manthey, Ulf-Dietrich Braumann, Ulrich Wolf, Gero Teichmann, Katrin Frauenschläger, Nadja Dornhöfer, Jens Eienkel

- Invasive neoplasms propagate locally within permissive compartments established in early embryogenesis and maintained during differentiation and maturation

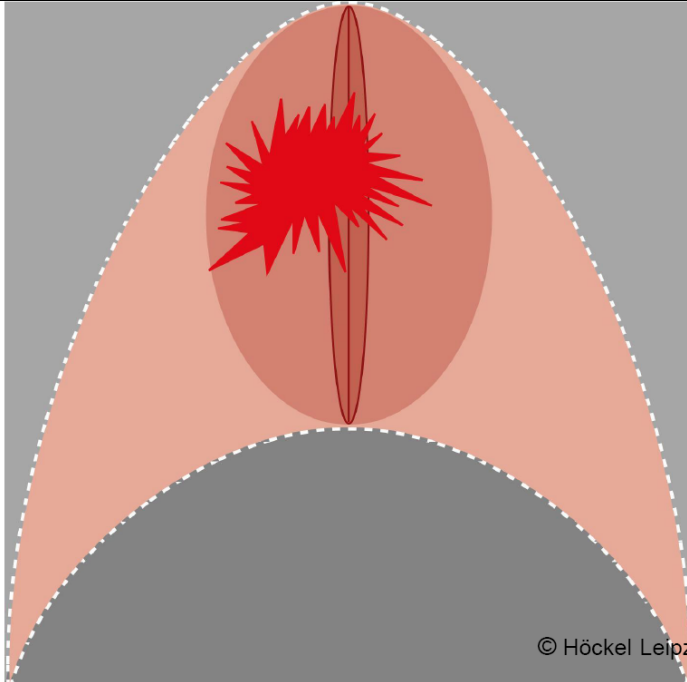
Local tumor spread **Compartment theory**

- Within the permissive compartment tumor spread is isotropic but compartment borders are functionally tumor suppressive

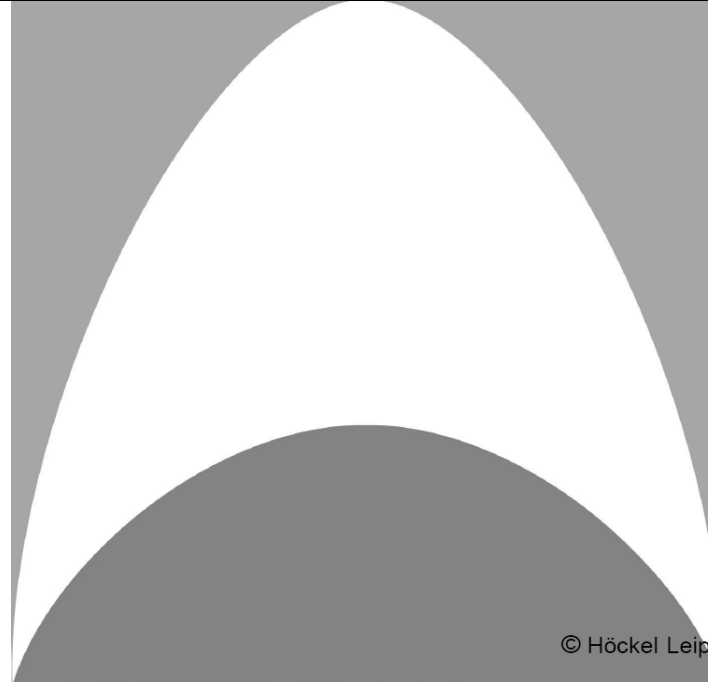


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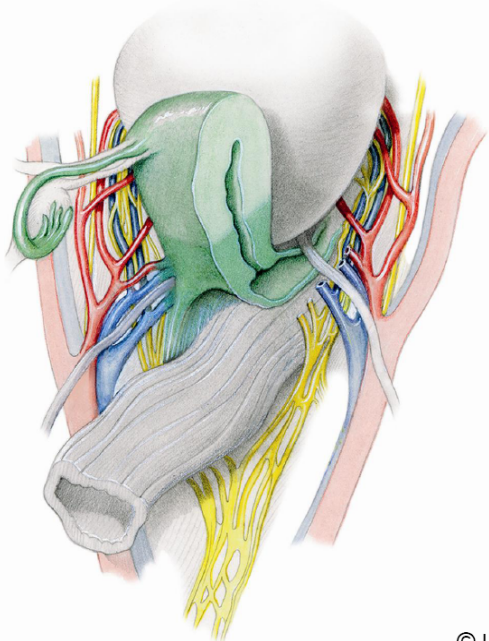
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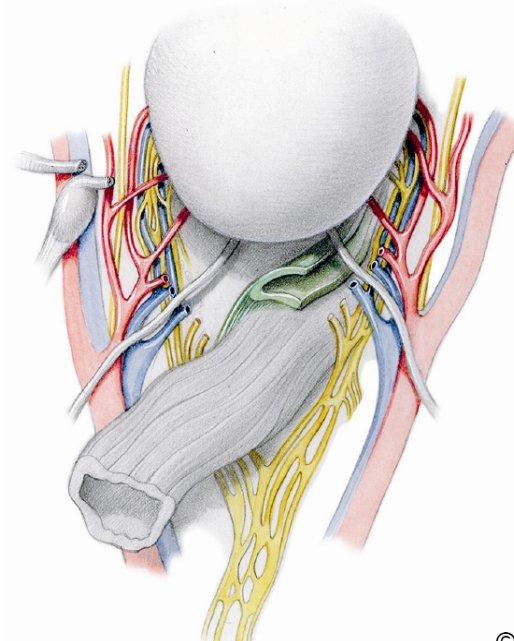
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TMMR supplement
Therapeutic pelvic LND

- 
- 219 consecutive FIGO stage IB1-2, IIA1-2, IB
 - NACT in patients with tumour size > 5 cm
 - No (!?) adjuvant radiotherapy
1. Recurrence pelvis 1.4%, pelvic + distant 1.1%, distant only 2.4%
 2. 5yr OS and DFS 96% and 94%
 3. 5yr OS and DFS in N+ (21%) 91% and 81%
 4. No grade 3-4 complications
 5. Grade 2 = 9%

Singol centre study!!!

Ongoing a german study

IJGC, 2007 May-Jun;17(3):623-8.

Ovarian metastases in early-stage cervical cancer (IA2-IIA): a multicenter retrospective study of 1965 patients (a Cooperative Task Force study)

Landoni et al.

Median age (years) 46 (range 16–84)

• FIGO stage	No.	%
Ia ₂	41	2
Ib ₁ – IIa	1084	64
Ib ₂ – IIa	570	34
• Histology squamous	1286	76
• LVSI +	672	40
• Positive lymph node	378	22
Ovarian mets	16	0,9

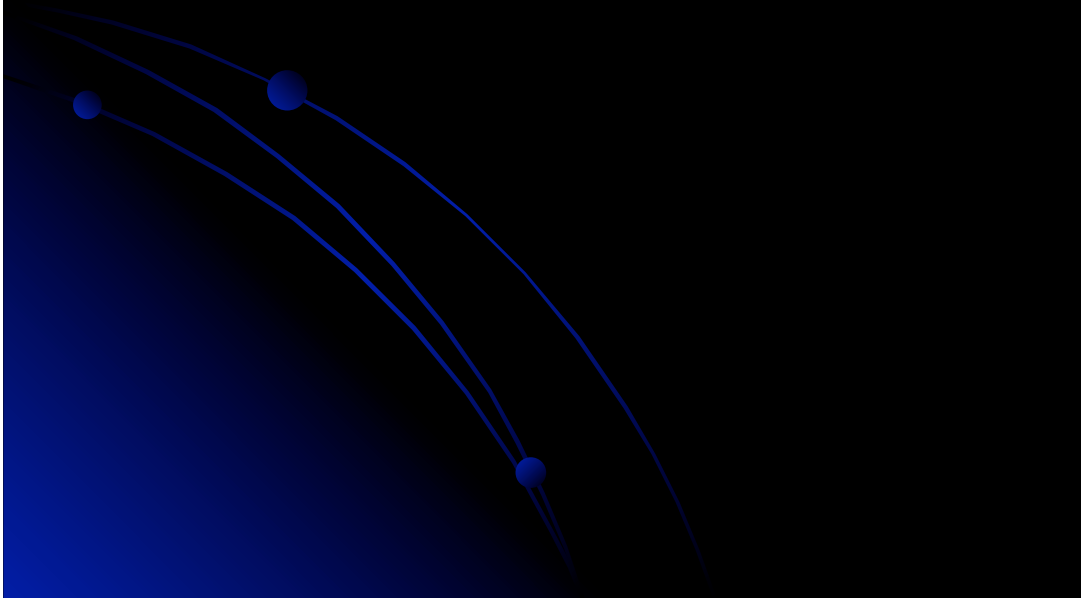
IA2, IB1 < 2 cm, less than $\frac{1}{2}$ of stromal invasion Parametrial Involvement?

How many LN negative pts have positive findings in the medial part of parametrium?

- Rob et al. 1999 – retrospective study 40 IA2, 85 IB1 - PI - 0%
- Covens et al. 2002 – retrospective study 3/536 - PI - 0,6%
- Steed et al. 2006 – retrospective study 0/120 - PI - 0%
- Plante et al. 2006 – radical trachelectomy 0/76 - PI - 0%
- Stegeman et al. 2007 – retrospective study 5/799 - PI - 0.63%

- Strnad P., Rob L et al. 2008 – prospective SLNM study
133 SLN neg. - PI - 0%
25 SLN posit. - PI - 28%!!

NACHTH tumor response



COMPARISON WITH SNAP-02

Characteristic	No.	%
<u>Age, yr</u>		
median	53	
range	(29-79)	
<u>Clinical FIGO stage</u>		
Ib2	2	1
IIb	54	40
IIb bulky	66	49
III-IVa	14	10
Hystological subtype		
Squamous cell carcinoma	131	96
Adenocarcinoma	5	4
Tumor grade		
1	3	3
2	23	24
3	39	41
NA ^a	31	32
missing data	40	29

	TP (80 patients)		TIP (74 patients)	
	n	%	n	%
Median age (25th–75 th percentiles), years	42 (36–49)		45 (39–51)	
Day 1 WHO performance status				
0	78	97.5	72	97.3
1-2	2	1.5	2	2.7
FIGO stage				
Ib2	45	56.2	47	63.5
IIa	14	17.5	10	13.5
IIb	16	20.0	14	18.9
III–IVa	4	5.0	3	4.1
Missing data	1	1.25	0	0
Tumour grade				
1	4	5.0	2	2.7
2	37	46.2	25	33.8
3	27	33.8	37	50.0
4	1	1.2	2	2.7
Missing data	11	13.8	8	10.8
Radiological lymph node involvement				
Yes	18	22.5	22	29.7

^aNot assessed because of pT0 or pT1 at post-chemotherapy surgery
 Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; TIP, paclitaxel, ifosfamide, and cisplatin; yr, year.

COMPARISON WITH SNAP-02

Parameter	No.	%
Post-chemotherapy pathological response		
CR	19	17
PR1	15	13
PR2	72	63
SD	7	6
PD	1	1

Response	Treatment			
	TP (<i>n</i> = 75)		TIP (<i>n</i> = 70)	
	<i>n</i>	%	<i>n</i>	%
CR	8	10.7	16	22.9
PR1	11	14.7	14	20.0
PR2	50	66.7	32	45.7
SD	5	6.7	6	8.6
PD	1	1.3	2	2.9

CONCLUSIONS

NEOADJUVANT TIP REGIMEN IS:

- **FEASIBLE** → 16% TREATMENT DELAY/WITHDRAWAL RATE,
93% RESECTION RATE
- **ACTIVE** → 30% PATH. OPTIMAL RESPONSE,
63% PATH. SUB-OPTIMAL RESPONSE

**EVEN IN AN HIGHER STAGE DISEASE ENRICHED SERIES THAN
REPORTED IN PREVIOUS CLINICAL TRIAL**

The present

EORTC protocol 55994

Randomized phase III study of neoadjuvant chemotherapy followed by surgery vs. concomitant radiotherapy and chemotherapy in FIGO Ib2, IIa > 4 cm or IIb cervical cancer.

Trial Status	Open
Dates	Date of activation: 19/03/2002
Data management at EORTC	Full
Phase	3
Randomized trial	Yes
Type	Neoadjuvant
Targeted Sample size	686
Number of steps	1
Drug	RADIOTHERAPY SURGERY
Study Staff	Nicoletta Colombo (Study Coordinator) - Istituto Europeo Di Oncologia, Milano Stefano Greggi (Study Coordinator) - Istituto Nazionale Per Lo Studio E La Cura Dei Tumori, Napoli Gemma Kenter (Study Coordinator) - Leiden University Medical Centre, Leiden Fabio Landoni (Study Coordinator) - Istituto Europeo Di Oncologia, Milano Corneel Coens (Statistician) - EORTC, Brussels Maarten De Rouck (Data Manager) - EORTC, Brussels An Demeester (Data Manager) - EORTC, Brussels
Type of cancer	Cervical
Participating Groups	EORTC Gynecological Cancer Group(Coordinating Group)