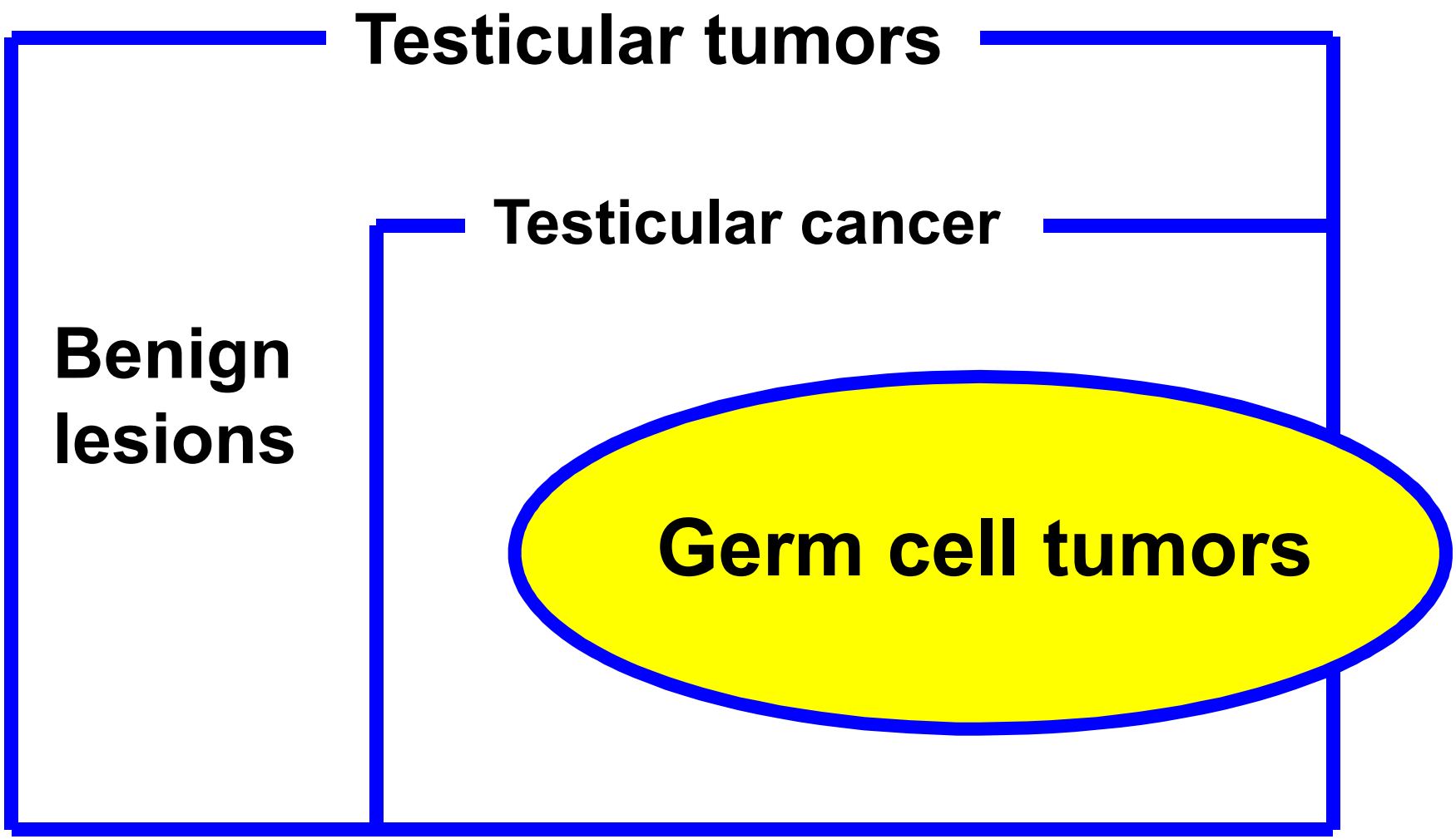
Testicular cancer

Terminology



Testicular cancer: Epidemiology I

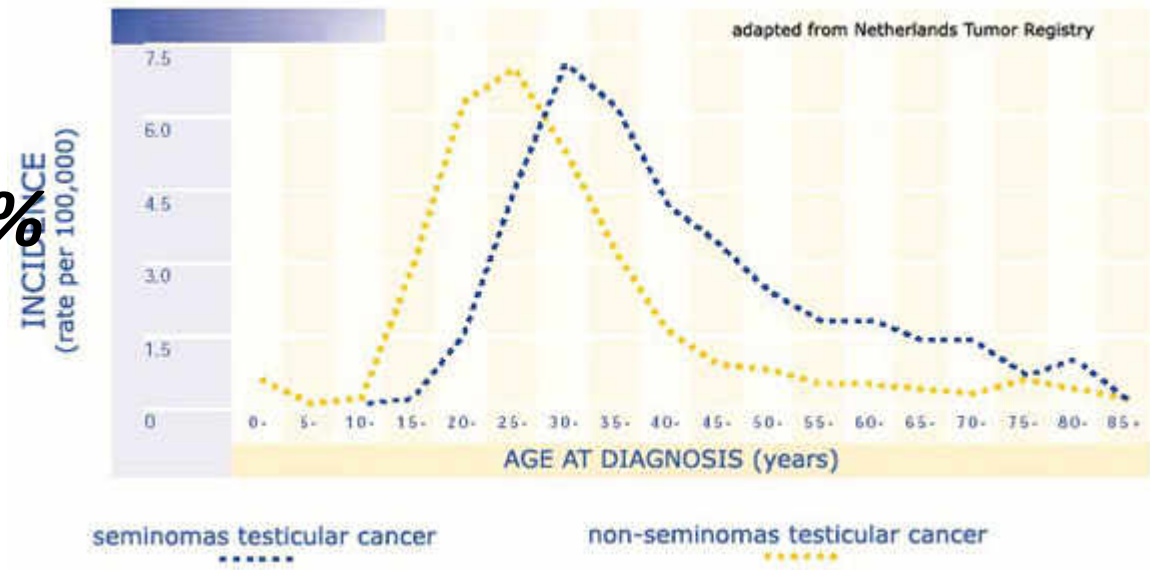
- The most common malignancy in men
  - in the 15-to 35 year-old age group
- Relatively rare among malignancies
  - 0,8-6,7 new cases annually per 100.000 males
- Incidence has raised recently

Testicular cancer: Epidemiology II

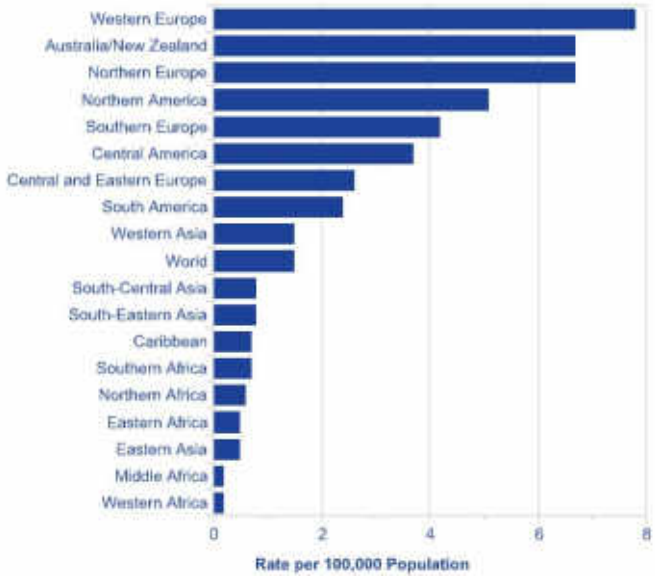
- Third leading cause of death due to malignant disease in this age group
- High rate of curability
  - Positive model for the multimodal treatment of malignancies

Overall: ***80-90%***

Low stage: ***95-100%***



Risk Factors I



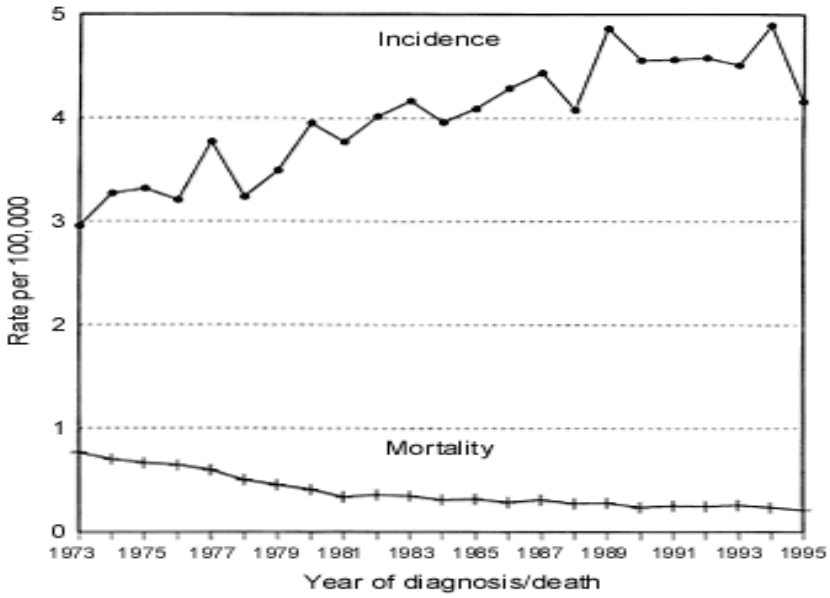
- The etiology of testicular cancer is unknown
- undescended testis (10x)
  - orchidopexy is not preventive
- in the American white (4x)
  - in USA compared to the American black
- estrogen for mother (3x)
  - during pregnancy

Risk factors (II)

- High society (2x)
  - higher incidence rates in upper socioeconomic classes of the American white
- the causative role of trauma and atrophy of the testis has not been proved
- no association with viruses

In the 1970's, significant discoveries stimulated both the diagnostical and the modern therapeutical approaches:

- therapy-related classification was introduced (by Mostofi)
- plasm and tissue level of AFP and HCG could be pointed out



- platinum based combined chemotherapy was introduced
- mapping of lymphatic system of the testis was performed
- the area of surgical intervention in retroperitoneal lymph nodes dissection was limited

Testicular Neoplasms

I. Germ Cell Tumors (~95%)

II. Stroma Cell Tumors (<5%)

- Leydig cell, Sertoli cell

III. Secondary Tumors of the Testis (rare)

- Lymphoma manifestations
- Metastatic tumors (prostate, lung, stomach)

IV. Other tumors

- Rete testis tu., Sarcoma,
- Mesothelioma, Androblastoma, etc.

Germ Cell Tumors

- Seminoma (35%)
- Embryonal carcinoma (20%)
- Teratoma (5%)
- Yolk sac tumor (rare)
  - Endodermal sinus tumor EDS
- Choriocarcinoma (rare)
- MIXED cell type (40%)

Tumor Spread

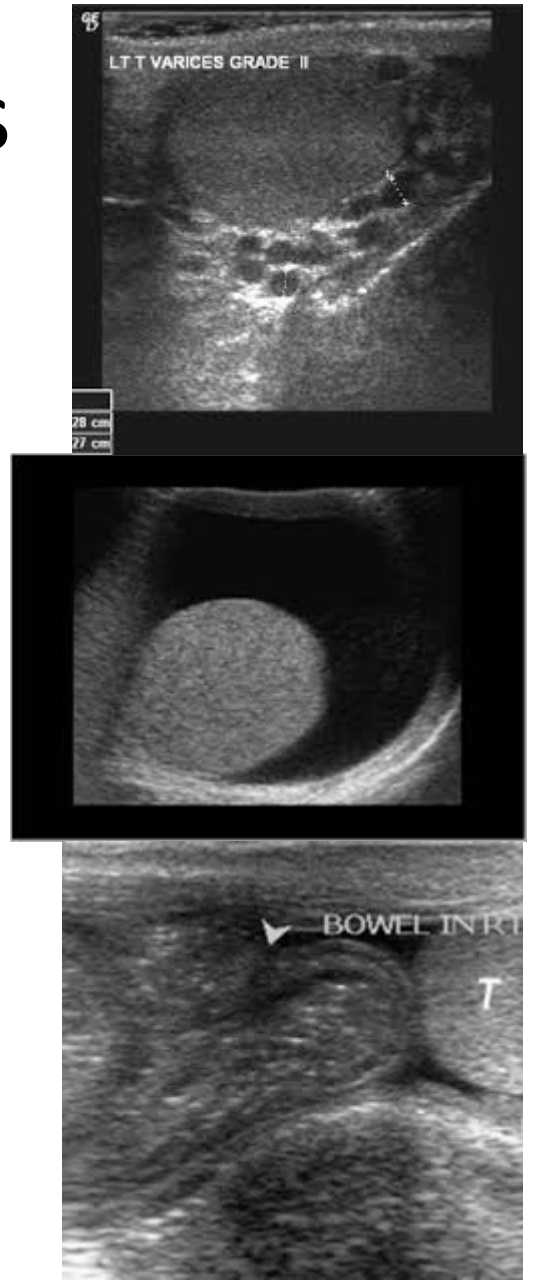
- Primary lymphogen spread
  - Periaortic and pericaval lymph nodes
    „Sentinel” lymph node: aorta and left renal vein angle
- Choriocarcinoma by blood
- Organ metastases
  - (1) lung
  - (2) liver, bones, brain, (worse prognosis)

Diagnostic procedures

- patient's history
  - symptoms of the primary or metastatic disease
- careful palpation of the testis and the abdomen
- rutin blood tests
  - including tumor markers (AFP, hCG, LDH)
- scrotal ultrasound (min. 5 MHz)
  - transillumination can be helpful if ultrasonography not available

Differential diagnosis „Intrascrotal Mass”

- testicular cancer
- epididimytis, orchitis
- hydrocele, hematocele
- varicocele
- torsion
- scrotal hernia



Symptoms of Testicular Tumor

- Painless enlargement of the testis
  - Without symptoms of inflammation
- Circumscribed hardness in testis
  - Detected frequently by sexual partner
- Oligo-asthenozoospermia
  - Detected by andrological examination

Symptoms of Metastatic Disease I

- „Unknown” retroperitoneal mass or supraclavicular lymph node enlargement
  - Detected incidentally by palpation or US
- Back pain
  - Tumorous compression of nerve roots

Symptoms of Metastatic Disease II

- Lower extremity swelling
  - Compression of vein cava inf.
- Hemoptoe, dyspnoe, cough
  - Caused by pulmonary metastases
- Gynecomastia
  - As a systemic endocrine manifestation

Testicular Tumor Markers

Specific

- Human Chorionic Gonadotropin (hCG)
- Alfa-fetoprotein (AFP)
- Placental Alkaline Phosphatase (PLAP)
- Placental lactogen
- Placental protein N°s 5,10,15
- Gamma-glutamine transpeptidase
- Cell surface antigens

Non specific

- Lactic dehydrogenase (LDH)
- Carcinoembryonic antigen (CEA)
- Polyamines (putrescine, spermin, spermidin)

What can the tumor markers be used for?

- for diagnostics
- for determination of clinical stage
- for following up the effectiveness of the therapy

Characteristics of AFP

- Glycoprotein
- Molecular weight: 70.000 D
- Biological „Half Life Time”: 5 days
- Measuring: RadioImmune-Assay
- Normal level: below 5 ng/ml

Characteristics of HCG

- Glycoprotein
- Molecular weight: 38.000 D
- Biological „Half Life Time”: 1 day
- Measuring: RadioImmune-Assay
- Normal level: below 5 mU / ml

Mandatory Examinations

- blood chemistry
  - including tumor markers (AFP, HCG, LDH)
- chest X-ray
- abdominal ultrasonography
- abdominal CT

Facultative Examinations

- Iv. Urography
- Chest CT
- Cavography (?)
- Radionucleid imaging
  - dynamic renography,
    brain, liver, bone scintigraphy
- Sperm analysis

Clinical Staging of Testicular Tumors (simplified)

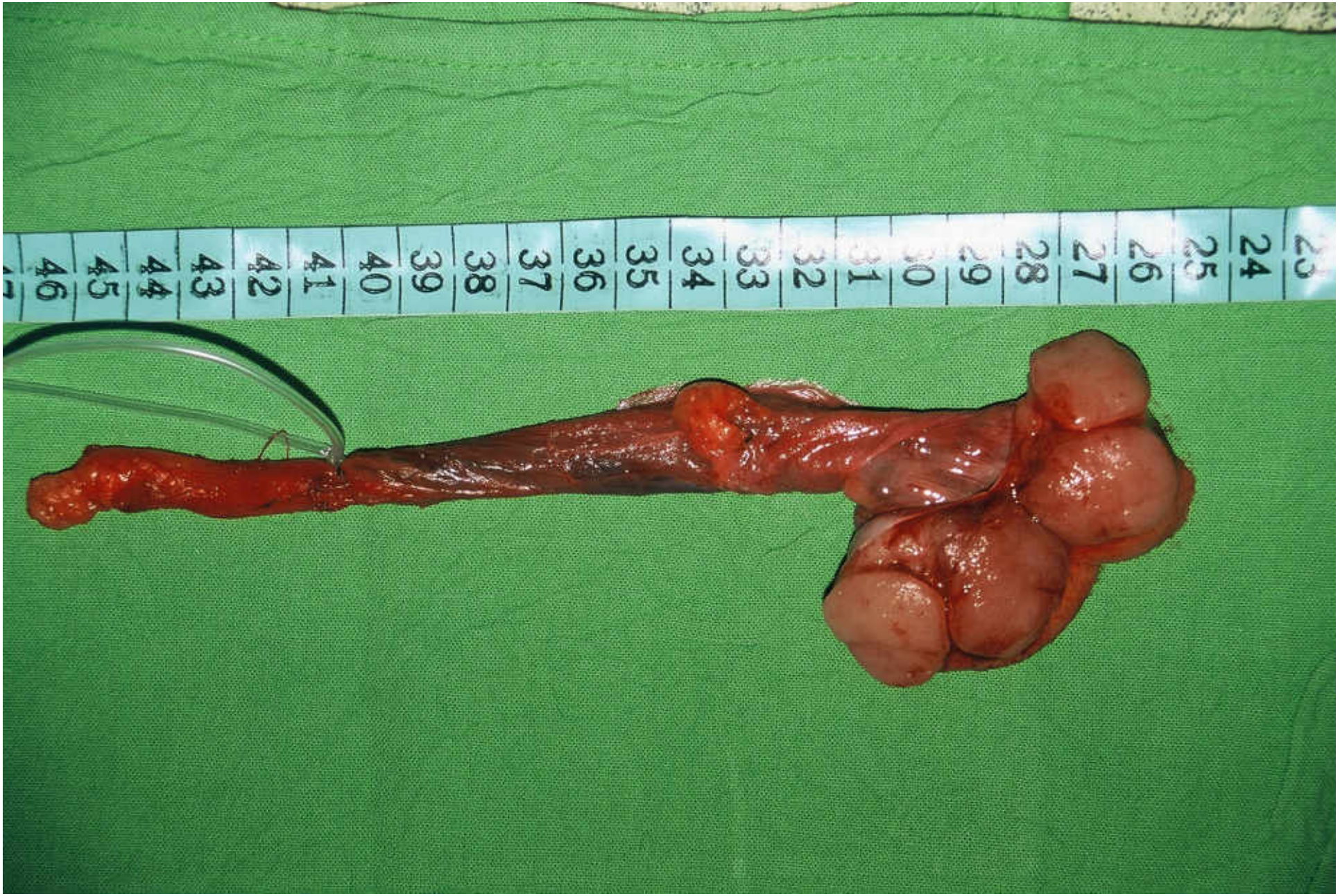
STAGE I	Tumor confined to testis
STAGE IIA	Regional lymph node metastasis < 2 cm
STAGE IIB	2-10 cm solitaire or multiplex
STAGE IIC („bulky”)	Over 10 cm in largest diameter
STAGE III	Extra regional lymph node or organ metastasis

Treatment of Testicular Cancer

- 1st step: Radical orchiectomy !

Treatment of Testicular Cancer

- 1st step: Radical orchiectomy
  - High inguinal incision
  - Cross clamp the spermatic cord
  - Remove testis with accessories and funiculus
- According to histology and stage
  - Surveillance: Wait and See
  - Radiation therapy
  - Chemotherapy
  - RPLND

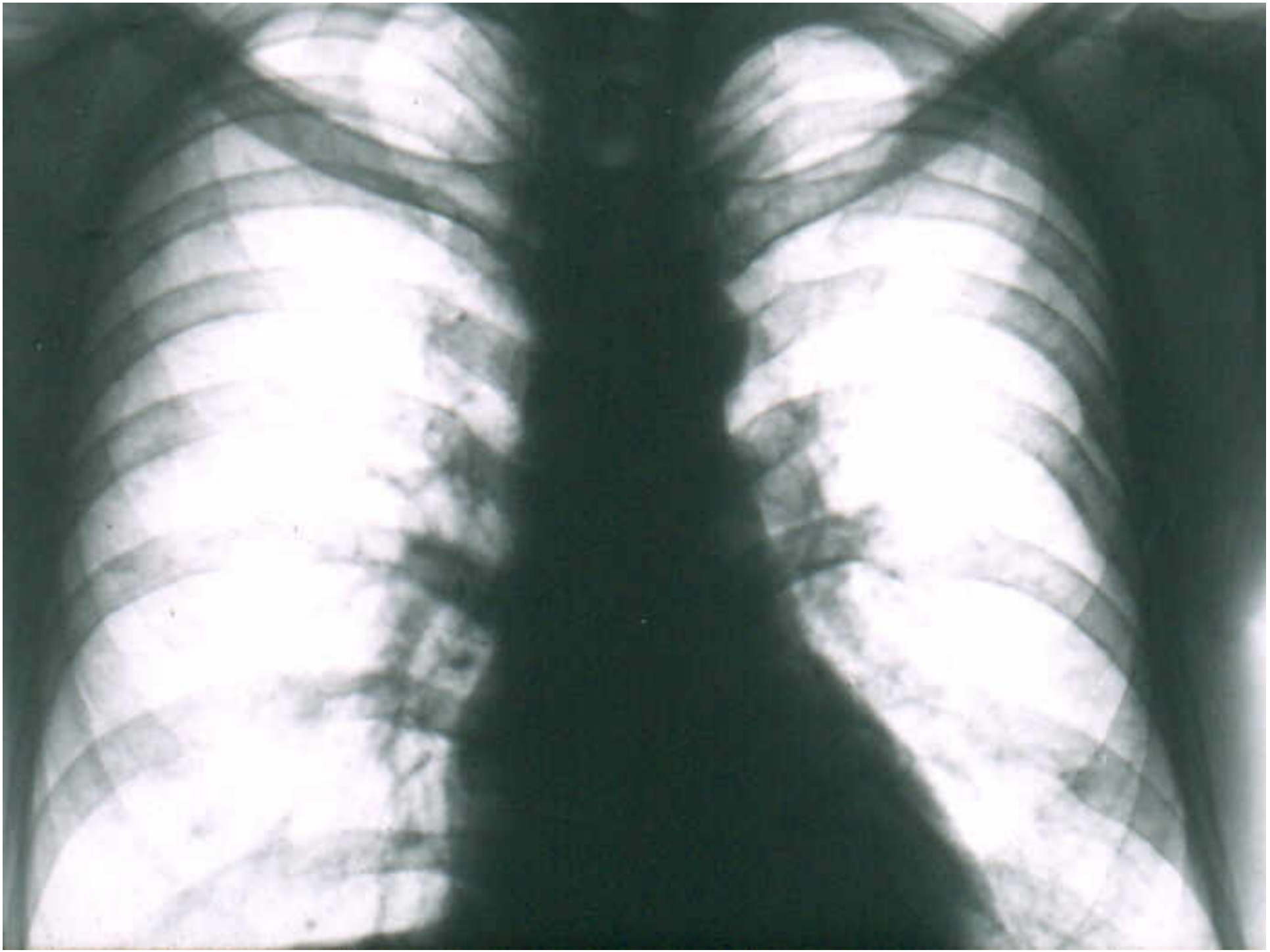


Radiotherapy of Testicular Cancer

- Seminoma is radiosensitive only
  - anaplastic variant is not radiosensitive
- „Ultra High Voltage” therapy is needed
- Microscopic or low volume metastasis can be treated (Stage I and II A)
- Investigations showed a 7 fold risk of 2nd malignancy 10 years after RT

Chemotherapy of Testicular Cancer

- Platinum based combination chemotherapy
  - has improved dramatically the survival of advanced TC
- PVB: Cisplatin, Vinblastin, Bleomycin
  - by Einhorn 1977
- PEB: Cisplatin, Etoposid, Bleomycin
  - by Williams 1987



Surgical therapy can be divided into 3 phases:

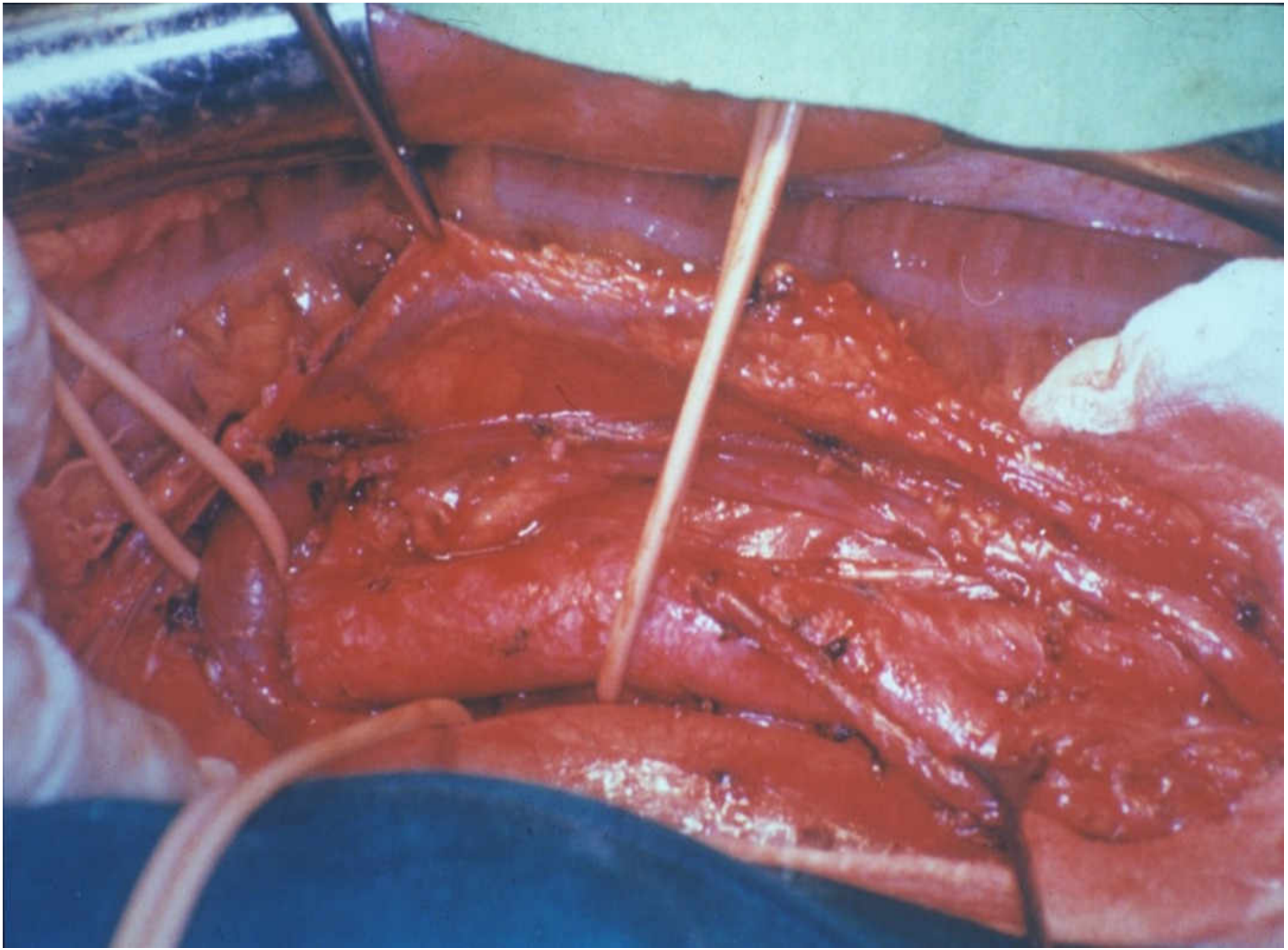
- Removal of primary tumor !!!
- Staging (debated)
- Removal of
  metastatic retroperitoneal lymph nodes

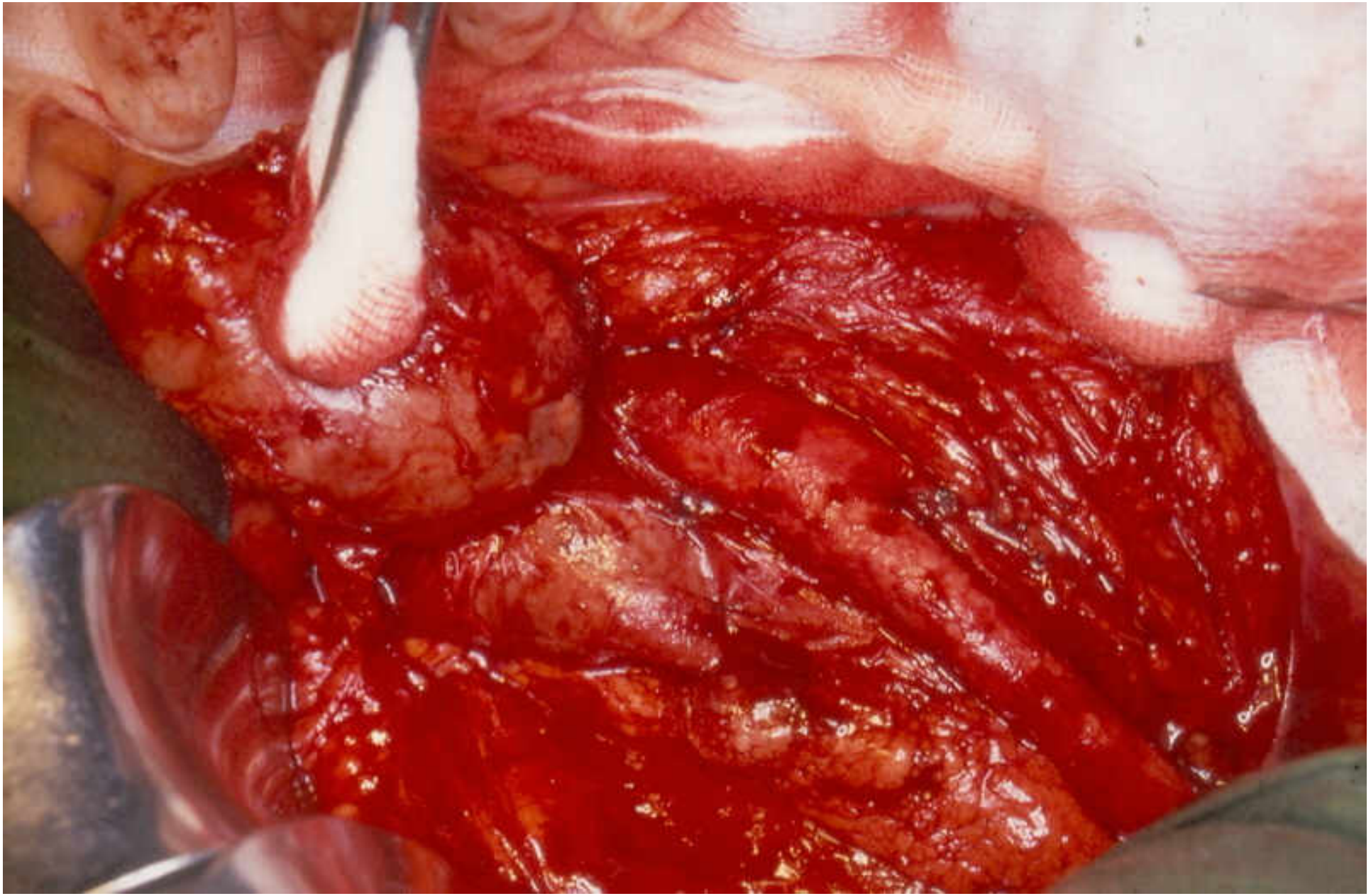
Major Indications of Performing RPLND

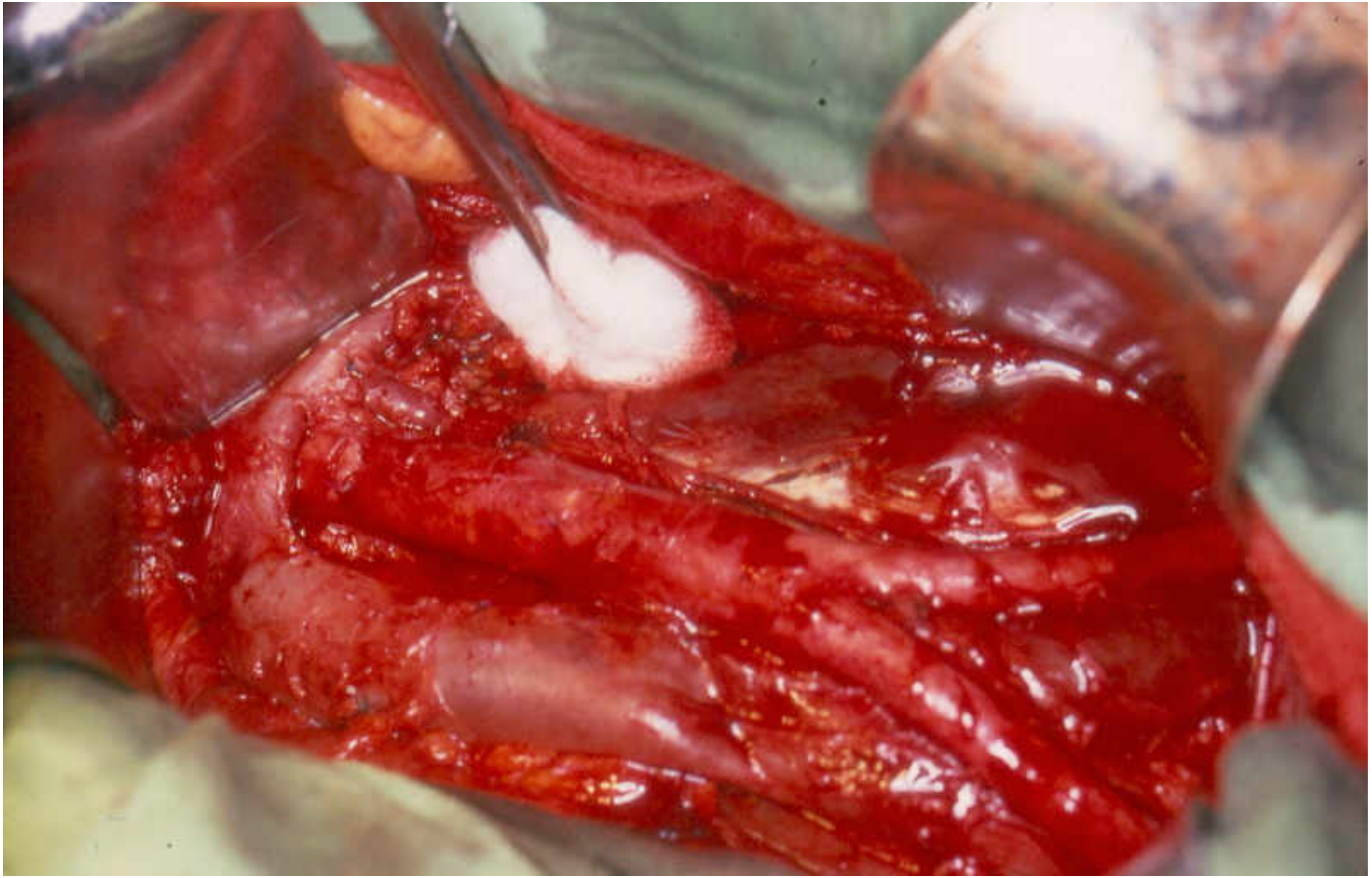
- (The estimation of the extension of the area involved by the malignant disease)
- (The reduction of the mass of tumor)
- Provides information about the impact of the previous irradiation or chemotherapy , i.e. about the options of further therapy

Different Types of RPLND

- (Primary RPLND
  - Bilateral, unilateral, nerve sparing)
- Salvage RPLND
  - Lymph node dissection after inductive chemotherapy
- Second look RPLND
  - Second dissection of primary unresectable masses after chemotherapy







Surveillance for Stage I NSGCT (orchiectomy alone)

- Rational
  - 75% of the Stage I patients receive „overtreatment” with RPLND, which morbidity could be avoided
- Conditions
  - careful staging, patient’s compliance, pT1 tumor without vascular invasion
- Disadvantages
  - relapsed cases (20-25%) should have received more aggressive treatment
    worse prognosis

Therapy of Low Stage Seminomas
UICC Stage I and IIA

- Radical orchiectomy
- Irradiation of retroperitoneal lymph nodes
  - with prophylactic or therapeutic dose
- Chemotherapy (single serie)
- Follow up care

Therapy of Advanced Seminomas UICC Stage IIB and above

- Radical orchiectomy
- Platinum based chemotherapy
  - 4 or 6 cycles
- Salvage RPLND in remission
  - for assessing residual mass
- Follow up care

Treatment Options of Stage I NSGCT

- Radical orchiectomy +
- Surveillance (orchiectomy alone)
  - 20-40% relapse
- (Primary RPLND debated
  - Unilateral or nerve sparing procedure)
- Chemotherapy 2 cycles of PVB

Treatment Options of Stage II („non-bulky”) NSGCT

- Radical orchiectomy +
- Inductive chemotherapy and salvage RPLND of residual masses if present
  - 4-6 cycles of PVB

Treatment of Advanced NSGCT (Stage II „bulky” and Stage III)

- Radical orchiectomy
- Inductive chemotherapy and salvage RPLND of residual masses in remission
- In selected cases: surgery of metastases after chemotherapy
  - brain, lung