Sordina IORT Technologies

IOeRT
Scientific Companion

Exploring the world of IOeRT
through publications,
facts & figures and illustrations.

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SIT IOeRT - Scientific Companion
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Introduction

Radiation therapy is a fundamental component of high-quality cancer care, with extensive evidence that about half of all cancer patients, wherever they live, could benefit from radiation therapy at least once during the course of their disease.
This first edition of IOeRT Scientific Companion offers a comprehensive introduction to the state of the art of research, clinics and scientific evidence on electron-based Intra Operative Radiation Therapy. Divided into thematic areas, the Companion provides you with up-to-date information about treatments defined and supported by guidelines issued by the most relevant scientific societies and treatments well established within the current clinical practice.
The first section of this publication offers a selection of readings concerning the use of IOeRT technique as defined in the guidelines drawn up by the most reputable scientific oncology societies. The second part summarises the most common applications according to current clinical practice and as described in the relevant literature. Bibliographic references are clearly listed and organised by anatomical district and treatment. A third section is currently being edited and will be included in a forthcoming issue of the Companion. This section will feature the most innovative and pioneering clinical and surgical solutions which are probably destined to inaugurate new fields of study and application.

This is an ideal and unmissable quick desktop reference guide for surgeons, oncologists, radiation oncologists, medical physicists, radiobiologists, radiation therapists and the wider oncology community.

The Companion, however, does not replace the original scientific articles and, above all, as happens for the guidelines themselves, cannot incorporate all possible clinical variations and is not intended to replace clinical judgement or individualisation of treatments.

IOeRT Applications Body Map

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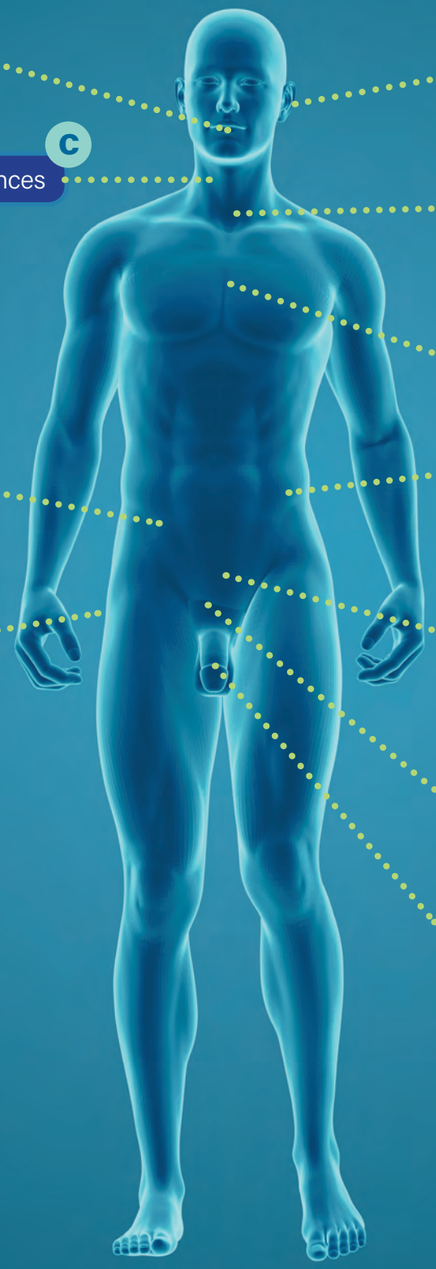

- Oral Surgery — NA
- Ear Surgery — NA
- Head and Neck — Oligo-Recurrences — C
- Esophago-Gastric — Resectable — C
- Esophago-Gastric — Stage II and III — C
- Gastric — Resectable — C
- Colon Cancer Locally Unresectable — N
- Renal — Recurrent/Primary resectable — C
- Rectal
  - cT2-4N+ — C
  - Primary and recurrent — C
  - Unresectable T4 — C
  - Recurrent — C
  - pT4N0/T1-4N+ — C
  - Primary locally advanced — E
  - Locally recurrent — E
  - Rectal Cancer Resectable — N
- Sarcoma — Retroperitoneal — C
- Sarcoma — Resectable Retroperitoneal — C
- Bladder Cancer — N
- ♂ Prostate — Metastatic D1 and D2 — C

♂♀ GENDER SPECIFIC

E ESTRO Guidelines · A ASTRO Guidelines · D DEGRO Guidelines

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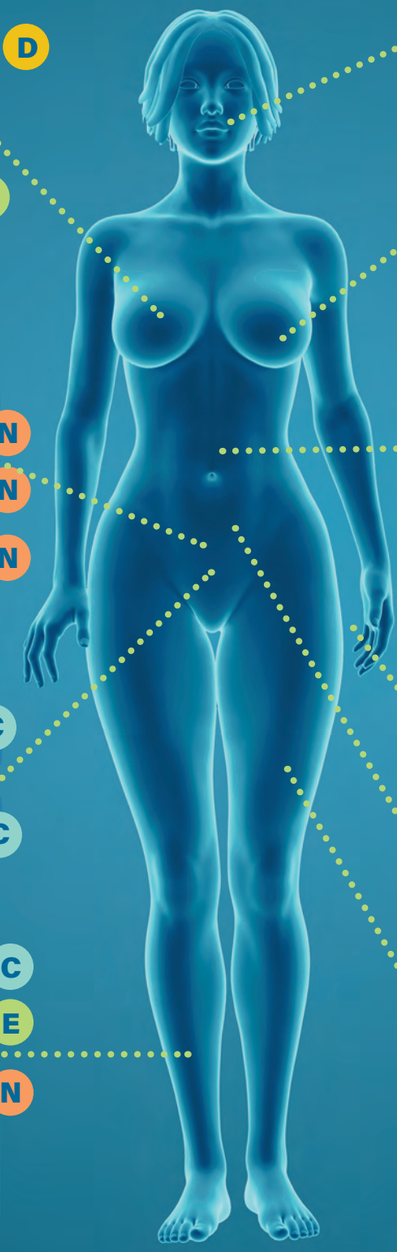


- ♀ Breast — Breast Cancer Single Dose — E A D
- ♀ Breast — Breast Cancer Boost — E
- Nasectomia — NA
- ♀ Breast Cancer with Cardiac Electronic Device — C
- Pancreas — Unresected — E N C
- Pancreas — Borderline — E C
- Pancreas — Recurrent cancer — N
- Pancreas — Resectable — C
- Pancreas — Unresectable or borderline-resectable — C
- ♀ Uterus — Endometrial Cancer Recurrent — N
- ♀ Uterus — Uterine Sarcoma — N
- ♀ Uterus — Cervical Cancer Recurrent — N
- Oligo-Recurrences — Rectal — C
- Oligo-Recurrences — Colorectal — C
- Oligo-Recurrences — Gynaecological — C
- Oligo-Recurrences — Uterine — C
- ♀ Pregnant — C
- Soft Tissues — Extremity Sarcoma — C
- Soft Tissues — Sarcoma — E
- Soft Tissues — Sarcoma (extremity, trunk, head-neck and retroperitoneal/intra-abdominal sarcoma) — N
- Sarcoma — Osteosarcoma — C

N NCCN Guidelines · C Current practice · NA New applications

Guidelines from oncological societies

All major oncological societies bring their active contribution to the daily fight against cancer issuing clinical practice guidelines, consensus documents and producing and disseminating other types of evidence-based or consensus-based documentation. Guidelines are developed to assist healthcare professionals and patients with cancer-related decision making activity. Because of their nature, guidelines as evidence-based documents, provides guidance on established applications. All guidelines are prepared based on information available ate the time literature review is conducted. The may vary over time and it is highly advisable to check for updates regularly.

ESTRO

European Society for Radiotherapy and Oncology

Founded in 1980, the **European Society for Radiotherapy and Oncology**, ESTRO, is a non-profit and scientific organisation dedicated to the advancement of all aspects of radiation oncology in order to improve patients' care in the multimodal treatment of cancer.

With over 6,500 members in and outside Europe, ESTRO supports all the radiation oncology professionals in their daily practice: radiation oncologists, medical physicists, radiobiologists, radiation therapists and the wider oncology community.

In order to achieve this, the Society promotes education, science dissemination and access to radiotherapy through its teaching courses, conferences, publications and public affairs activities.

Over the years, the steady expansion of the Society, anchored in the context of a continuously changing multidisciplinary oncology landscape, has asked for the formulation of new objectives, activities and structures for science dissemination, education and policy.

ESTRO's new vision statement for 2030 (*Radiation Oncology. Optimal Health for All, Together. ESTRO vision, 2030*) emphasises the ambition of the Society to further reinforce radiation oncology as core partner in multidisciplinary cancer care and to guarantee accessible and high-value radiation therapy for all cancer patients who need it.

Source: ESTRO web site www.estro.org

ASTRO

TARGETING CANCER CARE

ASTRO is the **American Society for Radiation Oncology**. A major radiation oncology society with a worldwide reach, ASTRO has more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals who specialise in treating patients with radiation therapies. These medical professionals, found at hospitals, cancer treatment centers and academic research facilities around the globe, make up the radiation therapy treatment teams that are critical in the fight against cancer. Together, these teams treat more than one million cancer patients each year. As a leading organisation in radiation oncology, the society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research and advocacy.

ASTRO provides members with the continuing medical education, health policy analysis, patient information resources and advocacy that they need to succeed in today's ever-changing health care delivery system.

Founded in 1958, ASTRO's mission is to advance the practice of radiation oncology by promoting excellence in patient care, providing opportunities for educational and professional development, promoting research and disseminating research results and representing radiation oncology in a rapidly evolving health care environment.

Source: ASTRO web site www.astro.org

German Society for Radiation Oncology

founded in 1995 as the scientific society of doctors, medical physicists and radiation biologists working in radiation oncology in Germany. Today it has around 2000 members. It is dedicated to radiation oncology in all its areas, including basic scientific research.

DEGRO is particularly committed to all tumour patients who need radiation treatment to heal or alleviate their symptoms. In order to give these patients the best possible prospects for a successful treatment, DEGRO focuses its efforts on quality-assured radiation oncology with the highest possible level of evidence.

That is why DEGRO promotes the scientific areas of radiation physics, radiation biology and clinical research, especially in the area of oncology, in order to be able to ensure an ever-improving and thus sustainable scientific basis for radiation oncology. The rules of good scientific practice, ethical norms and legal regulations are the basis here.

In addition, DEGRO takes care of the quality-assured implementation of scientific knowledge in medicine in patient treatment in all academic and non-academic clinics, medical care centers and practices so that all patients receive modern and safe radiation treatment.

DEGRO promotes further and advanced training for doctors working in radiation oncology in cooperation with state institutions and especially within the framework of its academy for advanced training in radiation oncology.

DEGRO takes care of the promotion of radiation oncology within next generation of doctors, especially through academic teaching activities addressed to medical students at universities, but also within the framework of the Young DEGRO, in which doctors, especially young medical physicists and biologists, have a special forum tailored on their specific age group.

In performing its tasks, DEGRO cooperates with a large number of other scientific medical specialist societies. In accordance with the interdisciplinary integration of radiation oncology in tumour treatment, DEGRO is involved in the development of evidence-based guidelines for the German Cancer Society and the AWMF, which play an essential role in ensuring reliable tumour therapy.

Source: DEGRO web site www.degro.org

National Comprehensive Cancer Network

NCCN The **National Comprehensive Cancer Network** is a not-for-profit alliance of 30 leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to improving and facilitating quality, effective, efficient, and accessible cancer care so patients can live better lives. Through the leadership and expertise of clinical professionals at NCCN Member Institutions, NCCN develops resources that present valuable information to the numerous stakeholders in the health care delivery system. By defining and advancing high-quality cancer care, NCCN promotes the importance of continuous quality improvement and recognizes the significance of creating clinical practice guidelines appropriate for use by patients, clinicians, and other health care decision-makers around the world.

World-renowned experts from NCCN Member Institutions diagnose and treat patients with a broad spectrum of cancers and are recognised for dealing with complex, aggressive, or rare cancers. NCCN Member Institutions pioneered the concept of the multidisciplinary team approach to patient care and conduct innovative research that contributes significantly to understanding, diagnosing, and treating cancer. NCCN programs offer access to expert physicians, superior treatment, and quality and safety initiatives that continuously improve the effectiveness and efficiency of cancer care globally.

Source: NCCN web site www.nccn.org

All data and information reported are taken from the mentioned NCCN guidelines and refer to the year 2018 unless otherwise indicated.

ESTRO Guidelines

Recommendations for intraoperative radiation therapy in **Unresected Pancreatic Cancer**

Recommendations for intraoperative radiation therapy in **Borderline-resected Pancreatic Cancer**

Recommendations for intraoperative radiation therapy in **Primary Locally Advanced Rectal Cancer**

Recommendations for intraoperative radiation therapy in **Locally Recurrent Rectal Cancer**

Recommendations for Intraoperative radiation therapy (IOeRT) for **Soft Tissue Sarcoma**

Recommendations for intraoperative radiation therapy with electrons (IORT) in **Breast Cancer**

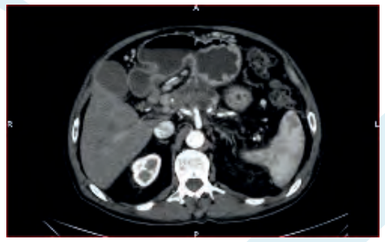
ESTRO Guidelines

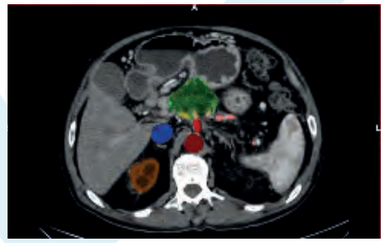
ESTRO IORT Task Force/ACROP

recommendations for intraoperative radiation therapy in **unresected pancreatic cancer**

District **Pancreas**

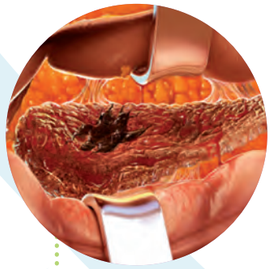
Indications Unresected Pancreatic Cancer



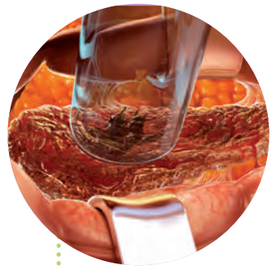


Radiation therapy (RT) is a valuable component of multimodal treatment for localized pancreatic cancer. Intraoperative radiation therapy (IOeRT) is a very precise and well-accepted asset in the clinical scenario and is extremely accurate in terms of dose-deposit characteristics and normal tissue sparing. It is a technique that can be integrated with systemic therapy and surgical progress. Unresectable disease categories benefit from dose escalated chemoradiation strategies in the context of active systemic therapy and potential radical surgery.

In this guideline, the ESTRO Task Force working group reports recommendations for performing IOeRT in unresected pancreatic cancer. These recommendations aim to define clinical indications, patient selection and technical aspects in a multidisciplinary setting in order to standardise treatment modalities across centres already using IOeRT, and to help institutions that intend to start IOeRT programmes for pancreatic cancer.



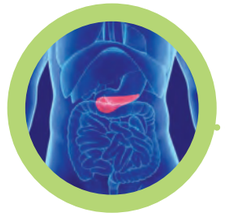
Pancreaticoduodenectomy involves the excision of the pancreatic head, duodenum, gallbladder and bile duct, with or without removal of the gastric antrum. Following resection, surgical manoeuvres are directed to assure direct access of the radiation beam to the primary lesi on, with temporarily positioning the stomach, transverse colon and duodenum out of the target volume.



Normal tissue at risk needs to be included in the target volume: biliary tree; pancreatic cancer involved parenchyma; vascular structures; retroperitoneal tissues; duodenum; coeliac plexus.

Bibliographic Reference

Calvo FA, Krengli M, Asencio JM, Serrano J, Poortmans P, Roeder F, Krempien R, Hensley FW. ESTRO IORT Task Force/ACROP recommendations for intraoperative radiation therapy in unresected pancreatic cancer. Radiother Oncol. 2020 Jul;148:57-64. doi: 10.1016/j.radonc.2020.03.040. Epub 2020 Apr 8. PMID: 32339779.



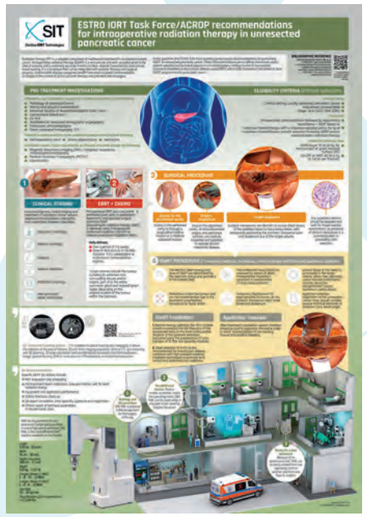
ESTRO Guidelines

ESTRO IOeRT Task Force/ACROP recommendations for intraoperative radiation therapy in **unresected pancreatic cancer**

ELIGIBILITY CRITERIA (Patient selection)

- DISEASE STATUS
  - Clinical setting: Locally advanced pancreatic cancer
  - Indications: Unresectable
  - Stage: IA-III (UICC TNM, 2016)
- TREATMENT
  - Preoperative chemoradiation followed by exploratory laparotomy + IOeRT boost *or*
  - Induction chemotherapy with a response-adapted policy for local treatment intensification patient selection including IOeRT and/or external beam radiation therapy
- RADIATION THERAPY DOSE
  - IOeRT boost 15 to 20 Gy for macroscopic or gross residual tumour (R2)
  - 3D-CRT or IMRT 45-50.4 Gy (in 1.8 Gy per fraction)

KEY MESSAGE



- Long-term survival and disease control are achievable in a proportion of well-selected patients with locally unresected pancreas cancer (OS 6% at 3 years; 3% >5 years).
- IORT, as part of a multimodality treatment plan for pancreas cancer, either locally advanced or unresected, has proven to promote high local control at the site of the primary tumour without a significant increase in treatment toxicity. With advances in the ability of systemic therapy to treat occult systemic metastases, the importance of sustained long-term local and regional control bears increasing interest, including in the expansion of the indications for IOeRT.
- As improvements are being made in distant disease control, the benefit of improved local control with regimens that include IOeRT may become even more decisive.

E ESTRO Guidelines

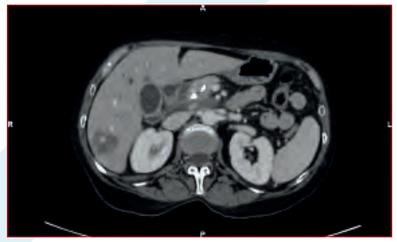
ESTRO IOeRT Task Force/ACROP

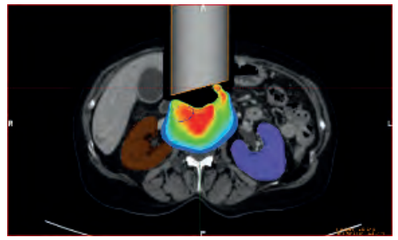
recommendations for intraoperative radiation therapy in **borderline-resected pancreatic cancer**

District **Pancreas**

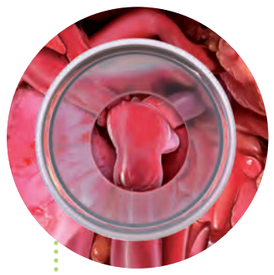
Indications Borderline Resected Pancreatic Cancer

Intraoperative radiation therapy (IOeRT) delivered with electrons is a very precise RT modality to intensify the irradiation effect for cancer involving upper abdominal structures and organs. Unresectable, borderline and resectable disease categories benefit from dose-escalated chemoradiation strategies in the context of active systemic therapy and potential radical surgery.
IOeRT is a well-accepted approach in the clinical scenario (maturity and reproducibility of results), and extremely accurate in terms of dose-deposition characteristics and normal tissue sparing. These are the ESTRO/ACROP recommendations for performing IOeRT in borderline-resectable pancreatic cancer.





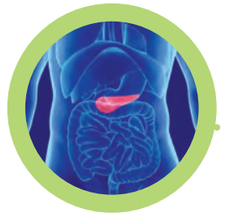
Pancreaticoduodenectomy involves the excision of the pancreatic head, duodenum, gallbladder and bile duct, with or without removal of the gastric antrum. Following resection, surgical manoeuvres are directed to assure direct access of the radiation beam to the primary lesi on, with temporarily positioning the stomach, transverse colon and duodenum out of the target volume.



Normai tissue at risk to be included in the radiation target volume: circumferential vasculature structures (inferior cava vein; portal vein; superior mesenteric artery and vein; aorta; ligated left gastric artery); lymphatic and retroperitoneal soft tissue; prevertebral ligament.

Bibliographic Reference

Calvo FA, Asencio JM, Roeder F, Krempien R, Poortmans P, Hensley FW, Krengli M. ESTRO IORT Task Force/ACROP recommendations for intraoperative radiation therapy in borderline-resected pancreatic cancer. Clin Transl Radiat Oncol. 2020 May 15;23:91-99. doi: 10.1016/j.ctro.2020.05.005. PMID: 32529056; PMCID: PMC7280753.



E ESTRO Guidelines

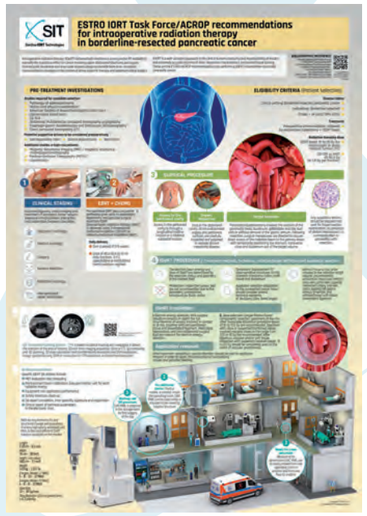
ESTRO IOeRT Task Force/ACROP recommendations for intraoperative radiation therapy in **borderline-resected pancreatic cancer**

ELIGIBILITY CRITERIA (Patient selection)

- DISEASE STATUS
  - Clinical setting: Borderline resected pancreatic cancer
  - Indications: Borderline/resected
  - Stage: > IA (UICC TNM, 2016)
- TREATMENT
  - Preoperative chemoradiation followed by exploratory laparotomy + IOeRT boost
- RADIATION THERAPY DOSE
  - IOeRT boost 15 to 20 Gy for macroscopic or gross residual tumour (R2)
  - 3D-CRT or IMRT 45-50.4

KEY MESSAGE

- Encouraging survival rates have been documented in patients treated with preoperative chemoradiation followed by radical surgery and IOeRT (>20 months median survival, >35% survival at 3 years).
- Intensive preoperative treatment, including induction chemotherapy followed by chemoradiation and an IOeRT boost, appears to prolong long-term survival within the subset of patients who remain relapse-free for>2 years (>30 months median survival; >40% survival at 3 years).
- Improvement of local control through higher RT doses has an impact on the survival of patients with a lower tendency towards disease spread.
- Extremely accurate in terms of dose-deposition characteristics and normal tissue sparing.



ESTRO Guidelines

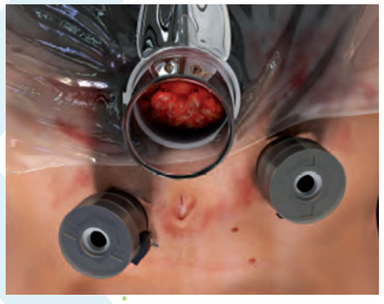
ESTRO/ACROP IOeRT recommendations for intraoperative radiation therapy in primary locally advanced rectal cancer

District **Rectal**

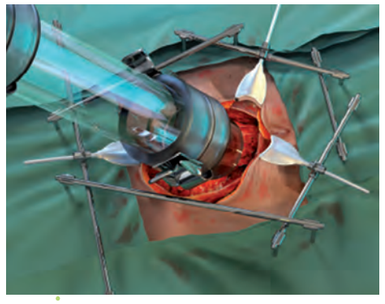
Indications Primary Locally Advanced Rectal Cancer

The treatment of locally advanced or clinical stage T4 primary rectal cancer has evolved aver the past 30 years. The current international consensus recognises the value of preoperative strategies with chemoradiation and the potential of IOeRT boost in cT4 patients. Progress in surgical methodology can incorporate an IOeRT component, which is feasible in laparoscopic approaches.

In this guideline/publication, the ESTRO Task Force reports recommendations for performing IOeRT in primary locally advanced rectal cancer (LARC). These recommendations aim to define clinical indications, patient-selection criteria and technical aspects in a multidisciplinary setting in order to standardise treatment modalities across centres already using IOeRT and to help institutions that intend to start IOeRT programmes for primary LARC.



Laparoscopic anterior-resection procedure: the retractar is assuring the exclusion of the rectal remant from the IOeRT field encompassing the presacral space.



Open IOeRt procedure: the multiple retractors exclude normal uninvolved organs and tissues (ureters, centro-pelvic organs, small bowel, etc.) from the target pelvic area.

Bibliographic Reference

Calvo FA, Sole CV, Rutten HJ, Poortmans P, Asencio JM, Serrano J, Aristu J, Roeder F, Dries WJ. ESTRO/ACROP IORT recommendations for intraoperative radiation therapy in primary locally advanced rectal cancer. Clin Transl Radiat Oncol. 2020 Sep 11;25:29-36. doi: 10.1016/j.ctro.2020.09.001. PMID: 33005755; PMCID: PMC7519207.

ESTRO Guidelines

ESTRO/ACROP IOeRT recommendations for intraoperative radiation therapy in primary locally advanced rectal cancer

ELIGIBILITY CRITERIA (Patient selection)

- DISEASE STATUS
  - Clinical setting: Primary locally advanced rectal cancer
  - Indications: Potentially Resectable
  - Stage: T3 – T4
- TREATMENT
  - Preoperative chemoradiation followed by resection + IOeRT boost
- RADIATION THERAPY DOSE
  - IOeRT boost: 10 – 12.5 Gy for negative resection margins (R0)
  - 12.5 – 15 Gy for microscopic positive resection margins (R1)
  - 15 to 20 Gy for macroscopic or gross residual tumour (R2)
- EXTERNAL BEAM RADIATION THERAPY (EBRT)
  - 45–50 Gy (in 25–28 fractions)

KEY MESSAGE

- The current international consensus recognises the value of preoperative strategies with chemoradiation and the potential of IOeRT boost in cT4 patients (NCCN, ESMO guidelines).
- Progress in surgical methodology can incorporate an IOeRT component, which is feasible in laparoscopic approaches.
- IOeRT is a feasible, tolerable, and efficient radiation-boosting technique that can be explored in tailored treatment for primary LARC patients.
- Recommendations for guiding tailoring of IOeRT in primary disease in terms of promoting local tumour control include the following:
  - The unfavourable nature of nodal and margin positivity together with no downstaging effects. IOeRT is an alternative for further dose-escalation and target volume redesign to improve local control under these conditions.
  - The tendency of T4 stage to recur in anterior pelvic structures, although IOeRT has also been reported to promote high local control rates in this disease category.
  - The excellent local results obtained in more favourable disease risk factors, which might make it advisable to reconsider the need for radiation treatment intensification and implement strategies with short-course preoperative pelvic irradiation including an IOeRT component.
  - The use of adjuvant chemotherapy should be recommended after IOeRT treatment in patients with proven adverse local features.

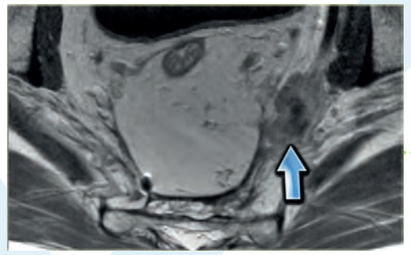
E ESTRO Guidelines

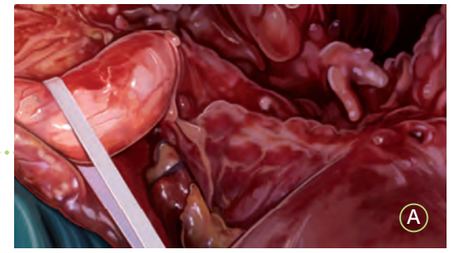
ESTRO/ACROP IORT recommendations for intraoperative radiation therapy in locally recurrent rectal cancer

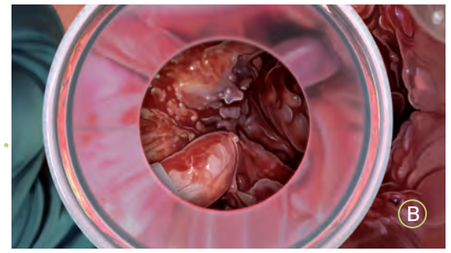
District **Rectal**

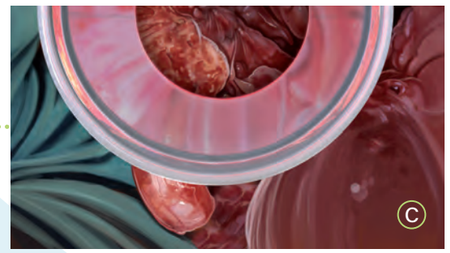
Indications Locally Recurrent Rectal Cancer

Although improvements in surgical technique and neoadjuvant therapy have significantly reduced the incidence of pelvic recurrence of rectal cancer, management of local recurrence remains problematic. A particularly challenging group of patients with locally recurrent rectal cancer includes those who have received a course of pelvic irradiation for their primary tumour or other pelvic malignancy, such as prostate or cervical cancer. The experience reported by expert IORT groups is reviewed and recommendations to guide clinical practice are explained in detail in the article presented here.









OeRT procedure view of a recurrent rectal cancer with associated uretero-hidronefrosis.

A - Pelvic cavity exposed and right ureteral dilatation.

B - IOeRT applicator positioning to treat recurrent tumor bed. The involved ureter is included in treatment.

C - The right ureter has been sectioned and mobilised.

Bibliographic Reference

Calvo FA, Sole CV, Rutten HJ, Dries WJ, Lozano MA, Cambeiro M, Poortmans P, González-Bayón L. ESTRO/ACROP IORT recommendations for intraoperative radiation therapy in locally recurrent rectal cancer. Clin Transl Radiat Oncol. 2020 Jun 17;24:41-48. doi: 10.1016/j.ctro.2020.06.007. PMID: 32613091; PMCID: PMC7320231.

E ESTRO Guidelines

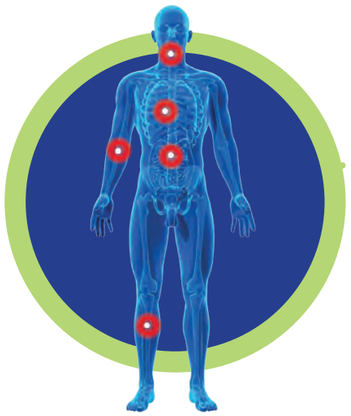
ESTRO/ACROP IOeRT recommendations for intraoperative radiation therapy in locally recurrent rectal cancer

ELIGIBILITY CRITERIA (Patient selection)

- DISEASE STATUS
  - Clinical setting: locally recurrent rectal cancer
  - Indications: Potentially Resectable, debulking surgery, oligometastatic
  - Dominant sites of involvement: Postero-lateral pelvic space
- TREATMENT
  - Preoperative chemoradiation followed by exploratory laparotomy + IOeRT boostt
- RADIATION THERAPY DOSE
  - IOeRT boost: 12.5–15 Gy for negative resection margins (R0)
  - 15–20 Gy for microscopic positive resection margins (R1)
  - 15 to 20 Gy for macroscopic or gross residual tumuor (R2)
- EXTERNAL BEAM RADIATION THERAPY (EBRT)
  - Full course 45–50 Gy (in 25–28 fractions)
  - Re-irradiation 25–35 Gy (12–15 fractions)

KEY MESSAGE

- The current international consensus recognises the value of preoperative strategies with chemoradiation and the potential of IOeRT boost in recurrent patients (NCCN guidelines).
- IOeRT is a feasible, tolerable and efficient radiation-boosting technique that can be explored in tailored treatment for patients with locally recurrent rectal cancer.
- Recommendations available to guide tailoring IOeRT in recurrent disease in terms of local tumour control promotion include implementing strategies with short-course preoperative pelvic irradiation, hypofractionated radiation or reirradiation, including an IOeRT component.



E ESTRO Guidelines

ESTRO IORT Task Force / ACROP

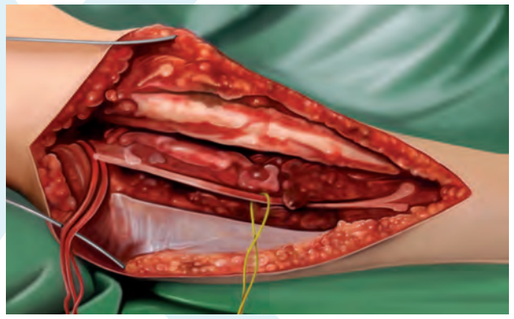
recommendations. Intraoperative radiation therapy (IORT) for Soft Tissue Sarcoma

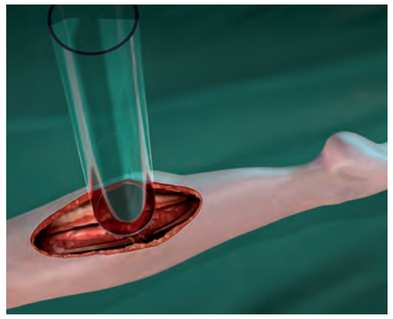
District **Soft Tissues**

Indications Sarcoma

Modern oncological concepts do not focus solely on the achievement of tumour control and survival but also on preservation of functionality and quality of life.
Combination of intraoperative radiation therapy (IOeRT) with pre- or postoperative external beam therapy results in excellent local control rates with good functional outcome in soft tissue sarcomas (STS).

In this guideline, the ESTRO Task Force working group reports recommendations for performing IOeRT for soft tissue sarcoma. These recommendations aim to define adequate patient selection criteria, incorporation into multimodal concepts, technical procedures, irradiation volumes, dose prescription, recording and reporting, treatment delivery and patient care for IOeRT procedures in adult patients with soft tissue sarcoma (STS).



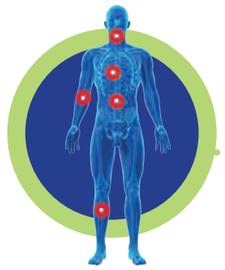


Normal tissues at risk to be included:
adjocent muscles/connective tissue structures, adjocent bone adjocent vessels (or grafts) in full thickness.

Normal uninvolved tissue to be excluded: *skin (mandotory), major nerves and bladder if technically and oncologically feasible, stomach and bowel structures, kidney and ureters.*

Bibliographic Reference

Roeder F, Morillo V, Saleh-Ebrahimi L, Calvo FA, Poortmans P, Ferrer Albiach C. Intraoperative radiation therapy (IORT) for soft tissue sarcoma - ESTRO IORT Task Force/ACROP recommendations. Radiother Oncol. 2020 Sep;150:293-302. doi: 10.1016/j.radonc.2020.07.019. Epub 2020 Jul 15. PMID: 32679306.



ESTRO IOeRT Task Force / ACROP
recommendations. Intraoperative radiation therapy (IOeRT) for Soft Tissue Sarcoma

ELIGIBILITY CRITERIA (Patient selection)

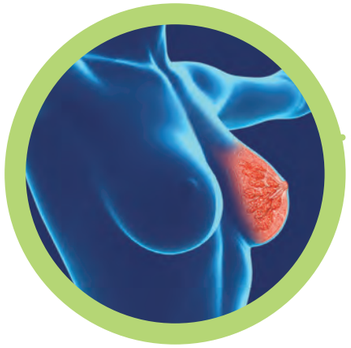
Extremity STS
RT is usually indicated in patients with high-risk features including high tumour grade, (anticipated) close or positive resection margin, tumour size >5cm, deep tumour location (in relation to the fascia) and locally recurrent disease.
If preoperative EBRT is planned, an additional IOeRT might be added if close or positive margins are found or assumed intraoperatively (based on the surgeons assessment or on frozen sections).
If postoperative EBRT is planned, an intraoperative boost can usually replace the external boost phase.

Retroperitoneal STS
The indication for EBRT is usually accepted for lesions with (anticipated) close or positive resections margins especially in the presence of other risk factors including tumour size > 5 cm, high tumour grade or locally recurrent disease.
EBRT should be done preoperatively and can be combined with an additional IOeRT boost if close or positive margins are found or anticipated intraoperatively (based on the surgeon's assessment or on frozen sections).

KEY MESSAGE

Extremity STS
Based on the available literature, the combination of limb-sparing surgery, IORT and EBRT results consistently in excellent 5-year local control rates of 82-97%.
The series reported by Tinkle et al. found 58% in recurrent cases. Those results seem at least equal to major non-IORT series, reporting 5-year LC rates of 83-93%, especially considering the higher proportions of patients with unfavourable prognostic factors in the IORT series.
Aside from direct oncological outcomes, IORT-containing approaches result consistently in very high limb preservation rates (81-100%) with good functional outcome (59-100%).

Retroperitoneal STS
Based on the available literature including data from prospective phase II studies, the combination of preoperative EBRT and IORT consistently results in high 5-year local control rates of 51-89%.
At least according to direct inter-study comparisons, those results seem to be superior to surgery alone or surgery combined with EBRT with regard to local control and in some series to overall survival.



E ESTRO Guidelines

ESTRO IORT Task Force/ACROP

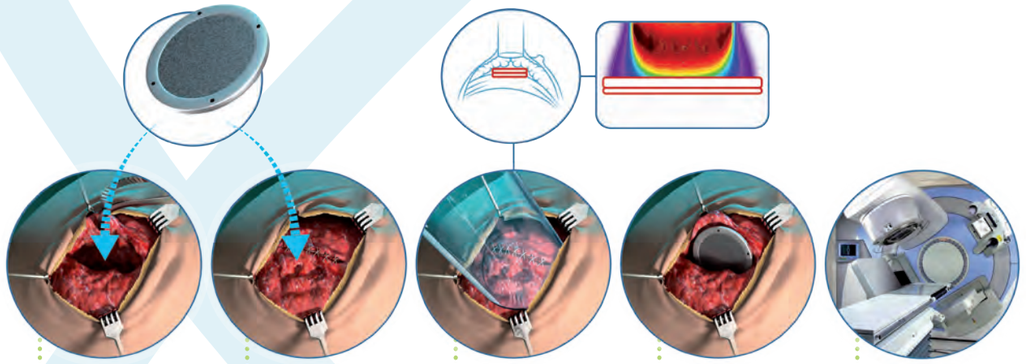
recommendations for intraoperative radiation therapy with electrons (IORT) in **breast cancer**

District **Breast**

Treatment Single Dose Boost

In 2020 ESTRO IORT Task Force/ACROP published their recommendation for intraoperative radiation therapy with electrons in breast cancer. The review provides a comprehensive overview of the role of intraoperative radiation therapy with electrons (IOeRT) in breast conserving therapy (BCT), both as partial breast irradiation (PBI) as well as anticipated boost (IOeRT boost).

Years of research and an endless clinical effort have demonstrated IOeRT as non-inferior to results of whole-breast irradiation in terms of local control, disease-free survival, overall survival and, in some aspects, superior regarding late side effects and quality of life.



Tissue mobilization and target preparation

Radioprotection disk is temporary inserted before irradiation and target volume is measured

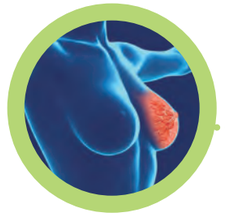
Applicator is docked and IOeRT dose is delivered

Applicator and radioprotection disk are removed

IOeRT-Boost
WBI can start as routinely when the wound is healed. WBI can be performed either with conventional fractionation, or with hypofractionation.

Bibliographic Reference

Fastner G, Gaisberger C, Kaiser J, Scherer P, Ciabattoni A, Petoukhova A, Sperk E, Poortmans P, Calvo FA, Sedlmayer F, Leonardi MC. ESTRO IORT Task Force/ACROP recommendations for intraoperative radiation therapy with electrons (IOERT) in breast cancer. Radiother Oncol. 2020 Aug;149:150-157. doi: 10.1016/j.radonc.2020.04.059. Epub 2020 May 13. PMID: 32413529.



E ESTRO Guidelines

ESTRO IOeRT Task Force/ACROP recommendations for intraoperative radiation therapy with electrons (IORT) in **breast cancer**

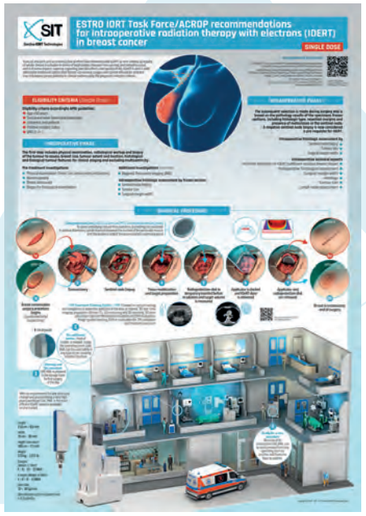
SINGLE DOSE

The largest evidence comes from Italian studies, especially the ELIOT randomised trial. Investigators showed that the rate of in-breast relapses (IBR) in the IOeRT group was significantly greater than with whole breast irradiation (WBI), even within the pre-specified equivalence margin. Tumour sizes >2 cm, involved axillary nodes, Grade 3 and triple negative molecular subtypes emerged as statistically significant predictors of IBR. For patients at low risk for in-breast recurrence (ASTRO/ESTRO recommendations), full dose IOeRT was isoeffective with standard WBI. Hence, several national guidelines now include this treatment strategy as one of the standard techniques for PBI in carefully selected patients.

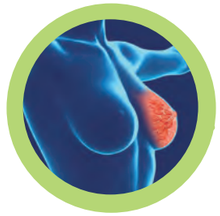
ELIGIBILITY CRITERIA according to APBI guidelines

- Age ≥50 years
- Ductal and other favourable histologies
- Unicentric and unifocal
- Positive receptor status
- pN0 (i-/i+)

KEY MESSAGE



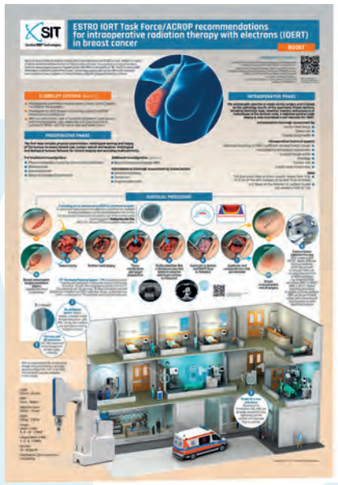
- Full dose IOeRT is a feasible APBI technique for patients with low-risk criteria.
- Acute and late toxicities are mild.
- IOeRT does minimally impair cosmetic outcome.
- Dose prescription and technical prerequisites are well established and described.



E ESTRO Guidelines

ESTRO IOeRT Task Force/ACROP recommendations for intraoperative radiation therapy with electrons (IOeRT) in breast cancer

BOOST



IOeRT Boost: The largest evidence for boost IOeRT preceding WBI comes from pooled analyses performed by the European Group of the International Society of Intraoperative Radiation Therapy (ISIORT Europe), where single boost doses (mostly around 10 Gy) preceded whole-breast irradiation (WBI) with 50 Gy (conventional fractionation). At median follow-up periods up to ten years, local recurrence rates around 1% were observed for low risk tumours. Higher local relapse rates were described for grade 3 tumours, triple negative breast cancer as well as for patients treated after primary systemic therapy for locally advanced tumours. Even in this settings, long-term (>5y) local tumour control rates beyond 95% were achieved. These encouraging results are interpreted as being attributable to utmost precision in dose delivery (by avoiding a "geographic and/or temporal miss"), and the possible radiobiological superiority of a single high dose fraction, compared to the conventionally fractionated boost.

ELIGIBILITY CRITERIA according to APBI guidelines

- Histologically confirmed invasive breast cancer clinical stages I-III (higher risk patients)
- Candidates for BCS (breast-conserving surgery) and WBI (whole breast irradiation)
- With no limits to the kind of systemic treatment (substances and time sequence), age, molecular sub-type (Luminal A, Luminal V, HER2+ and TN) tumour size and nodal status

KEY MESSAGE

- Reported systematic review shows that Boost-IOeRT plus WBI consistently resulted in high in-breast control rates, with observered 6- and 10-year local recurrence rates (LRR) of 0.8% and 2.7% respectively.
- In subgroups at "higher risk" for in breast recurrences (IBR), e.g. patients with locally advanced breast cancer (LABC) after primary systemic therapy (PST) or triple negative subtypes (TN), IOeRT Boost data compare favourably to those after other boost methods.

E ESTRO Guidelines

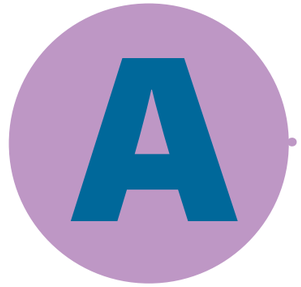
ESTRO IOeRT Task Force/ACROP recommendations for intraoperative radiation therapy with electrons (IOeRT) in breast cancer

IOeRT as Boost

STUDY	TREATMENT	LOCAL CONTROL
SEQUENTIAL INTERVENTION STUDY	External standard RT of 51-56.1 Gy (1.7 Gy per fraction) + **IOeRT BOOST (9 Gy at 90% isodose)**	**100%** 4.3 years follow up (1)
		98.4% 10 years follow up (2)
	External standard RT of 51-56.1 Gy (1.7 Gy per fraction) + **external BOOST of 12 Gy**	**95.7%** (1) 6.9 years follow up
		92.8% 10 years follow up (2)
ISIOeRT POOLED ANALYSIS	**IOeRT BOOST (10 Gy at 90% isodose)** + external standard RT of 50-54 Gy (1.7 Gy per fraction)	**99.2%** (3) 6 years follow up
CASE SERIES RESULTS OF A LOCALLY ADVANCED BREAST CANCER (LABC) POST INDUCTION CHEMOTHERAPY	**IOeRT BOOST (9 Gy at 90% isodose)** + external standard RT of 51-57 Gy (1.7-1.8 Gy per fraction)	**98.5%** (4) 5 years follow up
	External standard RT of 51-57 Gy (1.7-1.8 Gy per fraction) + external BOOST (12 Gy, 2 Gy per fraction)	**88.1%** (4) 5.7 years follow up
TRIPLE-NEGATIVE BREAST CANCER EXPERIENCE	**IOeRT BOOST (9.6 Gy median Dmax)** + external standard RT (median total dose of 54 Gy)	**93%** (5) 8.1 years of follow up
UPDATED 10-YEAR RESULTS OF UNSELECTED COHORT OF PATIENTS: CLINICAL STAGES I THROUGH III	**IOeRT BOOST (10 Gy at 90% isodose)** + external standard RT of 54 Gy (1.6-2 Gy per fraction)	**97.2%** (6) 10.1 years of follow up

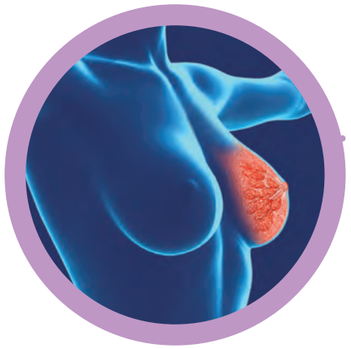
Bibliographic Reference

1. The Salzburg concept of intraoperative radiotherapy for breast cancer: Results and considerations, Reitsamer R. et al., Int. J. Cancer, Vol.118, pp. 2882–2887, 2006.
2. Fastner G, Reitsamer R, Kopp M, Menzel C, Glueck S, Merz F, et al. Intraoperative (IORT) versus external electron boost in breast conserving-operated breast cancer patients. 10-year results of a matched-pair analysis [Abstract]. Strahlenther Onkol. 2011;187:73–4
3. IOeRT with electrons as boost strategy during breast conserving therapy in limited stage breast cancer: Long term results of an ISIORT pooled analysis, Fastner G., Sedlmayer F., Ciabattoni A., Orecchia R., Valentini V. et al., Radiotherapy and Oncology, Vol. 108, Issue 2, pp. 279-286, 2013.
4. IOeRT as anticipated tumor bed boost during breast-conserving surgery after neoadjuvant chemotherapy in locally advanced breast cancer-Results of a case series after 5-year follow-up, Fastner G. et al., Int. J. Cancer, Vol. 136, pp. 1193–1201, 2015.
5. Survival and local control rates of triple-negative breast cancer patients treated with boost-IOeRT during breast-conserving surgery, fastenr G. et al., Strahlenther Onko, Vol.192, n.1, pp:1–7, 2016.
6. Intraoperative Tumor Bed Boost with Electrons in Breast Cancer of Clinical Stages I Through III: Updated 10-Year Results. Kaiser J, Kronberger C, Moder A, Kopp P, Wallner M, Reitsamer R, Fischer T, Fussl C, Zehentmayr F, Sedlmayer F, Fastner G. Int J Radiat Oncol Biol Phys. 2018 Sep 1;102(1):92-101. doi: 10.1016/j.ijrobp.2018.05.028.



ASTRO Guidelines

Accelerated Partial Breast Irradiation:
Executive summary for the update of
an **ASTRO Evidence-Based** Consensus Statement



A ASTRO Guidelines

Accelerated Partial Breast Irradiation: Executive summary for the update of an **ASTRO Evidence-Based** Consensus Statement

District **Breast**

Treatment Single Dose

In September 2016, ASTRO published the Update of the Accelerated Partial breast Irradiation (APBI) Consensus Statement in order to provide a guidance on use of IORT for Partial Breast Irradiation (PBI) in early stage breast cancer. On the basis of the published evidence and the mature results obtained thanks to the 5.8 years follow-up of the ELIOT trial, it has been recognized the efficacy of performing the IORT with electrons.

ELIGIBILITY CRITERIA

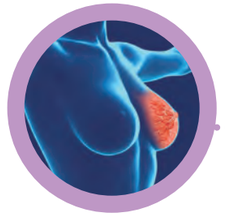
Age	≥ 50
Margins	Negative by at least 2mm
T Stage	Tis or T1
DCIS	If all of the below: - Screen detected - Low to intermediate nuclear grade - Size ≤ 2.5 cm - Resected with margins negative ≥ 3mm

KEY MESSAGE

- IOeRT with electrons (IORT) can be used in the clinical practice outside of a clinical trial for the suitable group of patients.
- IORT with low energy x-rays can never be used outside of a clinical trial.

Bibliographic Reference

Correa C, Harris EE, Leonardi MC, Smith BD, Taghian AG, Thompson AM, White J, Harris JR. Accelerated Partial Breast Irradiation: Executive summary for the update of an ASTRO Evidence-Based Consensus Statement. Pract Radiat Oncol. 2017 Mar-Apr;7(2):73-79. doi: 10.1016/j.prro.2016.09.007. Epub 2016 Sep 17. PMID: 27866865.



IOeRT as Single Dose

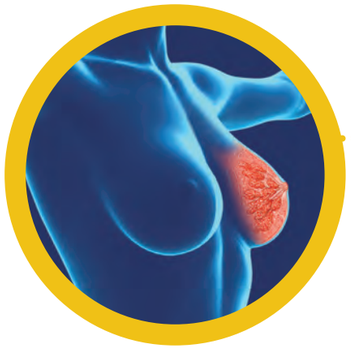
TREATMENT	PATIENTS SELECTION CRITERIA (LOW RISK GROUP)	LOCAL CONTROL
21 Gy prescribed at the 90% isodose	Suitable patients (low risk group) according to **ASTRO guidelines**	**98,5%** 5 years follow-up (1)
21 Gy prescribed at Dmax (18.9 Gy at the 90% isodose)	Suitable patients (low risk group) according to **ASTRO guidelines**	**99.6%** 46 years follow-up (2)
21 Gy prescribed at the 90% isodose	Good candidates (low risk group) according to **ESTRO guidelines**	**98.5%** 5 years follow-up (3)
21 Gy prescribed at the 90% isodose	Good candidates (low risk group) according to **ASTRO guidelines**	**98,8%** 5 years follow-up (4)

Bibliographic Reference

1. How Do the ASTRO Consensus Statement Guidelines for the Application of Accelerated Partial Breast Irradiation Fit Intraoperative Radiotherapy? A Retrospective Analysis of Patients Treated at the European Institute of Oncology, Leonardi M. C., Maisonneuve P, Mastropasqua G., Morra A., Lazzari R., Rotmensz N., Sangalli C., Luini A., Veronesi U., and Orecchia R., Int. J. Radiation Oncol. Biol. Phys., Vol. 83, No. 3, pp. 806-813, 2012.
2. Accelerated Partial Breast Irradiation using only intraoperative electron radiation therapy in the early stage breast cancer, Maluta S. et al., Int J Rad Onc, pp.1-8, 2012.
3. Accelerated partial breast irradiation with intraoperative electrons: Using GEC–ESTRO recommendations as guidance for patient selection, Leonardi M. C., Maisonneuve P., Mastropasqua M. G., Morra A., Lazzari R., Veronica D.A., Ferrari A., Rotmensz N., Sangalli C., Luini A., Veronesi U., Orecchia R., Radiotherapy and Oncology 106, pp. 21–27, 2013.
4. Breast cancer electron intraoperative radiotherapy: assessment of preoperative selection factors from a retrospective analysis of 758 patients and review of literature, Takenen S. et al., Breast Cancer Res Treat, 165(2):261-271, 2017.

DEGRO Guidelines

Practical guideline for **Partial-breast Irradiation**



D DEGRO Guidelines

DEGRO practical guideline for partial-breast irradiation

District **Breast**

Treatment Single Dose

In early 2020, theBreast Cancer Working Group of the German Society for Radiation Oncology (DEGRO) published a consensus statement aiming to define practical guidelines for accelerated partial-breast irradiation (APBI). Panel members of the DEGRO experts participated in a series of conferences, supplemented their clinical experience, performed a literature review, and formulated recommendations for implementing APBI in clinical routine, focusing on patient selection, target definition, and treatment technique.
The consensus statement presents the results of this complex effort in terms of appropriate patient selection, target definition and treatment technique to assure optimal results of APBI.

KEY MESSAGE

- In light of current data [...] IOeRT is described as "[...] a valid alternative treatment option after breast-conserving surgery and can be offered for carefully selected low-risk breast cancer patients in clinical routine using the proposed selection criteria."
- Several international guidelines have discouraged the use of 50-kV IORT outside of clinical trials. The DEGRO expert panel concluded that the **50-kV system cannot be recommended for routine adjuvant treatment of early invasive breast cancer after breast-conserving surgery and should preferentially be used in the context of a clinical trial.** Clinicians wishing to undertake APBI with 50-kV photons should ensure that patients understand the uncertainties about the procedure—particularly, patients should be counseled that follow-up is too short for general recommendations; that in corresponding clinical trial, still after very short not adequate follow-up, the risk of local recurrence was higher with APBI; and be informed about alternative treatment options. When used, it should be restricted to women with all of the following criteria: invasive cancer, aged >70 years, tumour <2cm, resection margins >2mm, grade 1—2, pN0, ER positive, HER2 negative, L0, V0, and EIC negative.

Bibliographic Reference

Strnad V, Krug D, Sedlmayer F, Piroth MD, Budach W, Baumann R, Feyer P, Duma MN, Haase W, Harms W, Hehr T, Fietkau R, Dunst J, Sauer R; Breast Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO). DEGRO practical guideline for partial-breast irradiation. Strahlenther Onkol. 2020 Sep;196(9):749-763. doi: 10.1007/s00066-020-01613-z. Epub 2020 Apr 29. PMID: 32350554; PMCID: PMC7449998.

NCCN Guidelines

Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Colon Cancer Version 4.2018 - October 19, 2018

Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Rectal Cancer Version 3.2018 - August 7, 2018

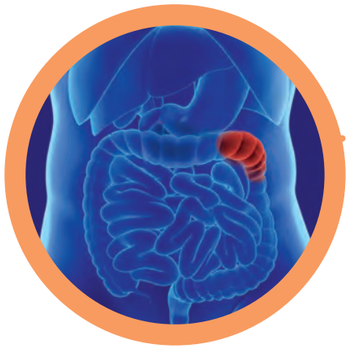
Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Bladder Cancer Version 1.2019 - December 20, 2018

Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Cervical Cancer Version 3.2019 - December 17, 2018

Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Pancreatic Adenocarcinoma Version 1.2019 - November 8, 2018

Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Soft Tissue Sarcoma Version 1.2019 - December 19, 2018

Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Uterine Neoplasms Version 2.2019 - December 17, 2018



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Colon Cancer Version 4.2018 - October 19, 2018

District **Colon**

Indications Locally Unresectable

Facts & Figures

NCCN Guideline reports **colorectal cancer** as the **fourth most frequently diagnosed cancer** and the second leading cause of cancer death in the United States.

95,270 new cases of colon cancer (estimated)

The incidence rate for colorectal cancer reported by the CDC for 2011 was 40.0 per 100,000 persons

43,030 cases of rectal cancer (estimated)

Mortality from colorectal cancer decreased by almost 35% from 1990 to 2007

50,630 people will die of colon and rectal cancer combined (36.6%)

The incidence of colorectal cancer in patients younger than 50 years has been increasing

The incidence of colon and rectal cancers per 100,000 people decreased from 60.5 in 1976 to 46.4 in 2005

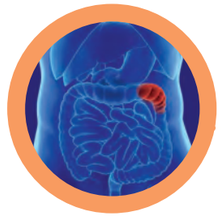
Incidence rates will increase by 90.0% and 124.2%, respectively, for patients 20 to 34 yrs by 2030

The incidence of colorectal cancer decreased at a rate of 2.9% per year between 2005 and 2014

The cause of this trend is currently unknown

PERIOPERATIVE CHEMORADIATION

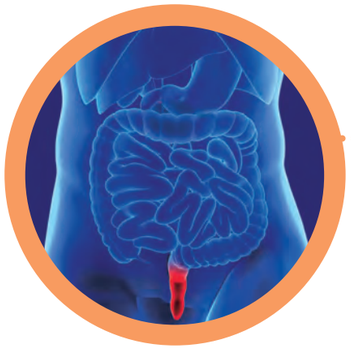
- Neoadjuvant or adjuvant radiation therapy delivered concurrently with 5-FU–based chemotherapy may be considered for very select patients with disease characterised as T4 tumours penetrating to a fixed structure or for patients with recurrent disease.
- Radiation therapy fields should include the tumour bed as defined by preoperative radiologic imaging and/or surgical clips.
- Intraoperative radiation therapy (IORT), if available, should be considered for these patients as an additional boost.



- If IORT is not available, an additional 10 to 20 Gy of external beam radiation therapy (EBRT) and/or brachytherapy could be considered to a limited volume.
- Chemoradiation can also be given to patients with locally unresectable disease or who are medically inoperable.
- In such cases, surgery with or without IORT can then be considered or additional lines of systemic therapy can be given.
- If radiation therapy is to be used, conformal beam radiation should be the routine choice; intensity-modulated radiation therapy (IMRT), which uses computer imaging to focus radiation to the tumor site and potentially decrease toxicity to normal tissue, should be reserved for unique clinical situations, such as unique anatomical situations or reirradiation of previously treated patients with recurrent disease.

PRINCIPLES OF RADIATION THERAPY

Intraoperative radiation therapy (IORT), if available, may be considered for patients with T4 or recurrent cancers as an additional boost. If IORT is not available, additional 10–20 Gy external beam radiation and/or brachytherapy could be considered to a limited volume.



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Rectal Cancer Version 3.2018 - August 7, 2018

District **Rectal**

Indications Locally Unresectable

Facts & Figures

NCCN Guideline reports **colorectal cancer** as the **fourth most frequently diagnosed cancer** and the second leading cause of cancer death in the United States.

43,030 cases of rectal cancer (estimated)

The incidence rate for colorectal cancer reported by the CDC for 2011 was 40.0 per 100,000 persons

25,920 cases in men

17,110 cases in women

Mortality from colorectal cancer decreased by almost 35% from 1990 to 2007

50,630 people will die of colon and rectal cancer combined (36.6%)

The incidence of colorectal cancer in patients younger than 50 years has been increasing

The incidence of colon and rectal cancers per 100,000 people decreased from 60.5 in 1976 to 46.4 in 2005

The authors estimate that the incidence rates for colon and rectal cancers will increase by 90.0% and 124.2%, respectively, for patients 20 to 34 years by 2030

The incidence of colorectal cancer decreased at a rate of 2.9% per year between 2005 and 2014

The cause of this trend is currently unknown

Recommendations for Patients with T3, N any Lesions with Involved CRM by MRI, with T4, N any Lesions, with Locally Unresectable Disease, or who are medically inoperable

- For patients with T4 tumours or recurrent cancers or if margins are very close or positive, intraoperative RT (IORT), which involves direct exposure of tumours to RT during surgery while removing normal structures from the field of treatment, may be considered as an additional boost to facilitate resection.
- If IORT is not available, 10 to 20 Gy and/or brachytherapy to a limited volume can be considered.

NCCN Guidelines

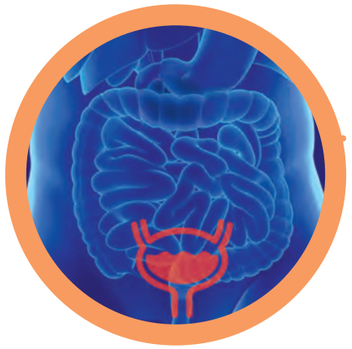
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Rectal Cancer Version 3.2018 - August 7, 2018

Treatment of Locally Recurrent Disease Locally recurrent rectal cancer is characterized by isolated pelvic/anastomotic recurrence of disease. [. . .]

- Patients with unresectable lesions should be treated with chemotherapy with or without radiation according to their ability to tolerate therapy.
- Debulking that results in gross residual cancer is not recommended. Potentially resectable isolated pelvic/anastomotic recurrence should be managed with preoperative chemo RT followed by resection (preferred if chemoRT was not previously given) or by resection followed by adjuvant chemoRT.
- IORT or brachytherapy should be considered with resection if it can be safely delivered.

PRINCIPLES OF RADIATION THERAPY

Intraoperative radiation therapy (IORT), if available, may be considered for very close or positive margins after resection, as an additional boost, especially for patients with T4 or recurrent cancers. If IORT is not available, 10–20 Gy external beam radiation and/or brachytherapy to a limited volume could be considered soon after surgery, prior to adjuvant chemotherapy.



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Bladder Cancer Version 1.2019 - December 20, 2018

District **Bladder**

Indications Stage IV A Cancer

Facts & Figures

NCCN Guideline reports **bladder cancer** as the **sixth most common cancer in the United States.** It is rarely diagnosed in individuals younger than 40 years of age.

81,190 new cases of urinary bladder cancer (estimated)

12,520 men

62,380 cases in men
18,810 cases in women

4,720 women

73 yrs — Given that the median age at diagnosis is 73 years, medical comorbidities are a frequent consideration in patient management

17,240 people will die of bladder cancer

The incidence of colon and rectal cancers per 100,000 people decreased from 60.5 in 1976 to 46.4 in 2005

The incidence of colorectal cancer decreased at a rate of 2.9% per year between 2005 and 2014

The clinical spectrum of bladder cancer can be divided into 3 categories that differ in prognosis, management, and therapeutic aims.

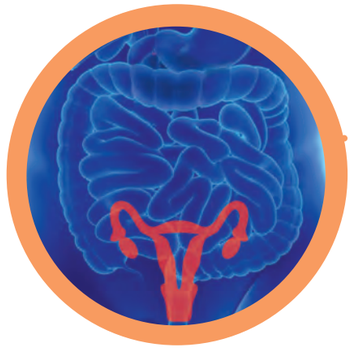
1 The first category consists of non–muscle-invasive disease, for which treatment is directed at reducing recurrences and preventing progression to a more advanced stage.

2 The second group encompasses muscle-invasive diseases. The goal of therapy is to determine whether the bladder should be removed or if it can be preserved without compromising survival, and to determine if the primary lesion can be managed independently or if patients are at high risk for distant spread requiring systemic approaches to improve the likelihood of cure.

3 The critical concern for the third group, consisting of metastatic lesions, is how to prolong quantity and maintain quality of life.

PRINCIPLES OF RADIATION MANAGEMENT OF INVASIVE DISEASE

In highly selected T4b tumour cases, may consider intraoperative RT.



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Cervical Cancer Version 3.2019 - December 17, 2018

District **Cervical**

Indications Recurrent

Facts & Figures

With 85% of cases occurring in developing countries - NCCN Guideline reports **cervical cancer** as a leading cause of cancer death in women (It **is the fourth most common cancer in women worldwide**).

13,240 new cases of carcinoma of the uterine cervix (estimated USA)

HPV — Persistent human papillomavirus (HPV) infection is the most important factor in the development of cervical cancer

4,170 USA — 4,170 people will die for this disease

Other epidemiologic risk factors associated with cervical cancer are a history of smoking, parity, oral contraceptive use, early age of onset of coitus, larger number of sexual partners, history of sexually transmitted disease, certain autoimmune diseases, and chronic immunosuppression

528,000 2012 GLOBAL — The global yearly incidence of cervical cancer in 2012 was 528,000 cases

266,000 GLOBAL — The annual death rate was 266,000 (or 50.4%)

It is the fourth most common cancer in women worldwide

80 / 20 — Squamous cell carcinomas account for approximately 80% of all cervical cancers, adenocarcinoma accounts for approximately 20%

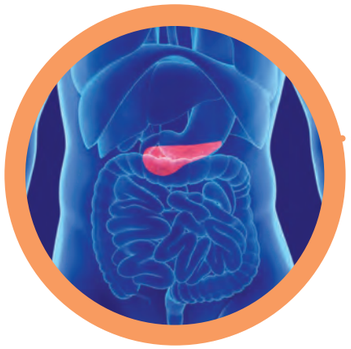
PRINCIPLES OF RADIATION THERAPY

Intraoperative Radiation Therapy

IORT is a specialised technique that delivers a single, highly focused dose of radiation to an at-risk tumor bed or isolated unresectable residual disease during an open surgical procedure. It is particularly useful in patients with recurrent disease within a previously radiated volume. During IORT, overlying normal tissue (such as bowel or other viscera) can be manually displaced from the region at risk. **IORT is typically delivered with electrons using preformed applicators of variable sizes matched to the surgically defined region at risk, which further constrains the area and depth of radiation exposure to avoid surrounding normal structures.** Patients with central pelvic recurrent disease after RT should be evaluated for pelvic exenteration, with (or without) intraoperative RT (IORT).

For patients with non-central recurrent disease, options include EBRT with (or without) chemotherapy, resection with (or without) IORT (category 3 for IORT), or chemotherapy (see the NCCN Guidelines for Palliative Care), or participation in a clinical trial.

All data and information reported are taken from the mentioned NCCN guidelines and refer to the year 2018 unless otherwise indicated



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Pancreatic Adenocarcinoma Version 1.2019 - November 8, 2018

District **Pancreas**

Indications Adeno-carcinoma

Facts & Figures

NCCN Guideline reports **pancreatic cancer** as the **fourth most common cause of cancer-related death among U.S. men and women.**

55,440 people will be diagnosed with pancreatic cancer (estimated)

The incidence of pancreatic cancer in the United States increased from 1999 to 2008

RISK FACTORS AND GENETIC PREDISPOSITION

Although the increase in risk is small, pancreatic cancer is firmly linked to cigarette smoking. Exposure to chemicals and heavy metals such as beta-naphthylamine, benzidine, pesticides, asbestos, benzene, and chlorinated hydrocarbons is associated with increased risk for pancreatic cancer as is heavy alcohol consumption. Periodontal disease is associated with pancreatic cancer, even when controlling for other risk factors such as gender, smoking, body mass index (BMI), diabetes, and alcohol consumption.

ADVANCED RADIATION TECHNIQUES

Intensity-modulated RT (IMRT) is increasingly being applied for therapy of locally advanced pancreatic adenocarcinoma and in the adjuvant setting with the aim of increasing radiation dose to the gross tumor while minimizing toxicity to surrounding tissues. To date there is no clear consensus on the appropriate maximum dose of radiation when IMRT technique is used.

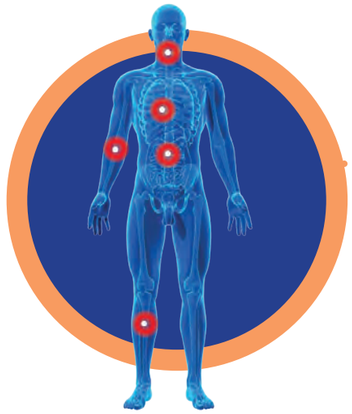
Intraoperative RT (IORT) can allow for higher doses of radiation because sensitive structures can be excluded from the radiation fields. IORT is sometimes administered to patients with borderline resectable disease who have received maximal neoadjuvant therapy to sterilize close or involved margins at the time of surgery.

It is also sometimes used when a patient is found to be unresectable at the time of surgery and in cases of locally recurrent disease.

Most studies of IORT in patients with locally advanced pancreatic cancer found that while local control may be improved, no change in survival is evident with use of IORT because of the high frequency at which metastatic disease develops.

Some groups, however, believe that IORT can offer benefits in very carefully selected patients with non-metastatic disease.

Overall, there is no clear established role for IORT in patients with pancreatic cancer and the panel believes it should only be performed at specialized centers.



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Soft Tissue Sarcoma Version 1.2019 - December 19, 2018

District **Soft Tissue**

Indications Sarcoma

Facts & Figures

Sarcomas constitute a heterogeneous group of rare solid tumours of mesenchymal cell origin with distinct clinical and pathologic features; they are usually divided into two broad categories:

- Sarcomas of soft tissues (including fat, muscle, nerve and nerve sheath, blood vessels, and other connective tissues)
- Sarcomas of bone

The NCCN Guidelines® for Soft Tissue Sarcoma address the management of STS in adult patients from the perspective of the following disease subtypes:

- STS of extremity, superficial/trunk, or head and neck
- Retroperitoneal or intra-abdominal STS
- GISTs
- Desmoid tumours (aggressive fibromatoses)
- RMS

The anatomic site of the primary disease represents an important variable that influences treatment and outcome.

Trunk 10%

Extremities 43%

Visceral 19%

Head and neck 9%

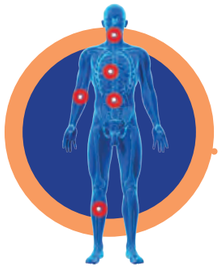
Retroperitoneum 15%

Sarcomas collectively account for approximately 1% of all adult malignancies and 15% of pediatric malignancies

13,040 people will be diagnosed with soft tissue sarcoma (STS)

5,150 will die because of STS

More than 50 different histologic subtypes of STS have been identified



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **Soft Tissue Sarcoma** Version 1.2019 - December 19, 2018

SURGERY

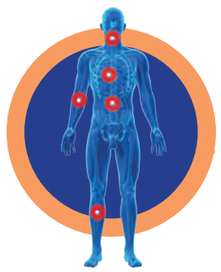
Positive surgical margin is a strong predictor of LR for patients with extremity STS. Microscopically positive margins are associated with a higher rate of LR and a lower rate of DFS in patients with extremity sarcomas Collectively, the data suggest that limb-sparing surgery with or without postoperative RT is an effective treatment option for extremity STS and amputation should be reserved only for cases where resection or reresection with adequate margins cannot be performed without sacrificing the functional outcome. The guidelines recommend that the goal of surgery for patients with STS of extremities should be functional limb preservation, if possible, within the realm of an appropriate oncologic resection.

RADIATION THERAPY

RT can be administered either as primary, preoperative, or postoperative treatment. Total RT doses are always determined based on the tissue tolerance. Newer RT techniques such as brachytherapy, **intraoperative RT (IORT)**, and intensity-modulated RT (IMRT) have **led to the improvement of treatment outcomes in patients with STS**.

IORT

Recent reports from a retrospective study suggest that **IORT provides excellent local control to STS of the extremity.** Recently it has been reported **long-term outcome of patients with STS of upper extremity treated with EBRT**, surgery, and **IORT**. The 10-year local control and OS rates were 88% and 58%, respectively. The 10-year local control rates were 89% and 86%, respectively, following margin-negative (R0) and margin-positive (R1 and R2) resections. IORT was also retrospectively examined in cohorts of patients with STS of the superficial trunk or extremity who received surgery, IORT, and EBRT at 3 Spanish institutions. Five-year IORT in-field control was 86% and 70% for extremity and trunk wall STS, respectively. However, 5-year DFS was 62% in the extremity STS cohort and 45% in the trunk wall STS.
Incomplete resection significantly impacted in-field control in both cohorts, and higher IORT dose was positively associated with in-field disease control in extremity STS.



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **Soft Tissue Sarcoma** Version 1.2019 - December 19, 2018

Radiation Therapy Guidelines for Soft Tissue Sarcoma of Extremity/Trunk/Head-Neck

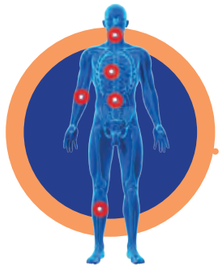
PRINCIPLES OF RADIATION THERAPY FOR SOFT TISSUE SARCOMA

Potential benefits of preoperative radiation therapy:

- Lower total radiation dose
- Shorter course of treatment
- Treatment field size is frequently smaller
- Associated with less late radiation toxicity and improved extremity function
- The primary sarcoma is a defined target for radiation treatment planning
- Treatment delivery not impacted by postoperative wound healing issues
- Potential downstaging of borderline resectable extremity sarcomas for possible limb salvage
- Ability to restage patients after preoperative radiation but before wide resection
- Distant metastases would prevent a noncurative surgery

Preoperative RT

- 50 Gy external-beam RT (EBRT)4 (surgery with clips to follow)
- Following preoperative 50 Gy EBRT and surgery, for positive margins, consider observation or RT boost
- If using RT boost, consider: 6,7
  - EBRT:
    - 16–18 Gy for microscopic residual disease 5,8
    - 20–26 Gy for gross residual disease5
  - Brachytherapy (low-dose rate):
    - 16–18 Gy for microscopic residual disease
    - 20–26 Gy for gross disease
  - Brachytherapy (high-dose rate):
    - 14–16 Gy at approximately 3–4 Gy BID for microscopic residual disease
    - 18–24 Gy for gross residual disease
  - IORT:
    - 12.5 Gy for microscopic residual disease
    - 15 Gy for gross residual disease



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **Soft Tissue Sarcoma** Version 1.2019 - December 19, 2018

Radiation Therapy Guidelines for Soft Tissue Sarcoma of Extremity/Trunk/Head-Neck

PRINCIPLES OF RADIATION THERAPY FOR SOFT TISSUE SARCOMA

Potential benefits of postoperative radiation therapy:

Allow for definitive pathologic assessment, including margin status, where there was not a definitive indication for preoperative radiation.

Lower rate of postoperative wound healing complications, especially the lower extremity.

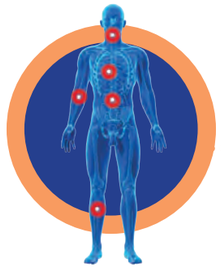
Postoperative RT following surgery with clips.

- EBRT (50 Gy) + EBRT boost4,6
  - Boost Dose
    - Negative margins: 10–16 Gy
    - Microscopically positive margins: 16–18 Gy
    - Gross residual disease: 20–26 Gy

Preoperative RT

- IORT (10–16 Gy) + EBRT (50 Gy)
- Brachytherapy ± EBRT
  - Positive margins: 5
    - Low-dose-rate (16–20 Gy) or high-dose-rate equivalent (14–16 Gy) brachytherapy + 50 Gy EBRT6
  - Negative margins: 5
    - 45 Gy low-dose-rate or high-dose-rate equivalent (ie, 36 Gy in 3.6 Gy BID over 10 fractions in 5 days)6 brachytherapy

Based on the pros and cons of preoperative versus postoperative radiation, the panel has expressed a general preference for preoperative radiation.



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **Soft Tissue Sarcoma** Version 1.2019 - December 19, 2018

Radiation Therapy Guidelines for Retroperitoneal/ Intra-Abdominal Sarcoma12,13

RETRO PERITO NEUM

Surgical resection of a localized tumor with negative margins remains the standard, potentially curative treatment for patients with retroperitoneal/intra-abdominal STS. Postoperative margin status is the most important factor contributing to long-term DFS.

PRINCIPLES OF RADIATION THERAPY FOR SOFT TISSUE SARCOMA

Preoperative RT

Preoperative RT is often preferred, because it reduces the risk of tumour seeding at the time of surgery and may render tumors more amenable to resection.

NCCN recommends 50 Gy preoperative RT (in 1.8–2 Gy per fraction), followed by surgery with clips and consideration of IORT boost for positive margins.

Postoperative RT

The data regarding the survival benefits of postoperative RT are conflicting.

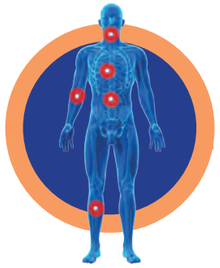
If postoperative RT is deemed necessary in highly selected cases, a coordinated effort by the surgeon and the radiation oncologist to displace bowel from the tumour bed with omentum or other tissue displacers is recommended to reduce the risk of RT-related bowel toxicity.

Intraoperative Radiation Therapy

The use of IORT has provided encouraging results in patients with retroperitoneal STS.

In patients with retroperitoneal STS prospectively treated at a single institution with a protocol involving maximal tumour resection, HDR IORT, and postoperative EBRT, the overall 5-year local control rate for the whole group was 62%; local control rate was better for patients with primary tumours than for those with recurrent tumors (74% vs. 54%; P = .40).

The overall 5-year distant metastasis-free survival rate was 82% (100% for those with low-grade tumours vs. 70% for those with high-grade tumours; P = .05).



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **Soft Tissue Sarcoma** Version 1.2019 - December 19, 2018

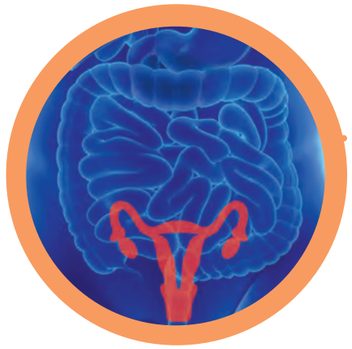
Radiation Therapy Guidelines for Retroperitoneal/ Intra-Abdominal Sarcoma12,13

RETRO PERITO NEUM

The 5-year DFS and OS rates were 55% and 45%, respectively. IORT with or without EBRT has been effective in terms of local control and survival in patients with primary and recurrent retroperitoneal STS.

In a study that assessed the long-term outcome of patients with retroperitoneal STS treated by preoperative RT, resection, and IORT with intraoperative electron beam RT (IOERT), OS (74% and 30%, respectively) and local control (83% and 61%, respectively) were better in patients undergoing gross total resection and IOERT compared to those who had only gross total resection.

An ongoing study (NCT01566123) is examining preoperative RT, followed by surgery with IORT in patients with high-risk retroperitoneal sarcoma. Preliminary results suggest promising local control and OS rates.



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **Uterine Neoplasms** Version 2.2019 - December 17, 2018

District **Uterus**

Indications Neoplasms

Facts & Figures

Adenocarcinoma of the endometrium (also known as endometrial cancer, or more broadly as uterine cancer or carcinoma of the uterine corpus) is the most common malignancy of the female genital tract in the United States. The NCCN Guidelines for Uterine Neoplasms describe malignant epithelial tumors and uterine sarcomas; each of these major categories contains specific histologic groups that require different management.

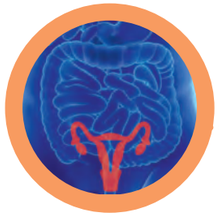
63,230 — It is estimated that 63,230 new uterine cancer cases will occur in 2018 in USA

11,350 † USA — 11,350 deaths will result from the disease

3% — Stromal or mesenchymal sarcomas are uncommon subtypes accounting for approximately 3% of all uterine cancers.

Risk factors for uterine neoplasms include

- Increased levels of estrogen
- late age at menopause
- Early age at menarche
- Lynch syndrome
- Older age (≥55 years)
- Use of Tamoxifen



NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **Uterine Neoplasms** Version 2.2019 - December 17, 2018

Treatment of Recurrent or Metastatic Disease

Localised Disease

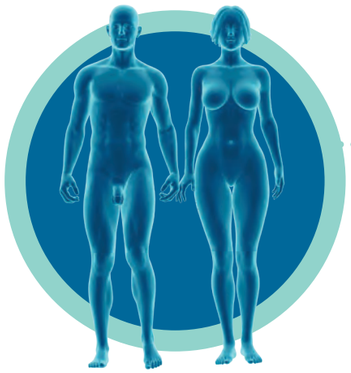
For patients previously treated with brachytherapy only at the recurrence site, surgery with (or without) intraoperative RT (IORT) is recommended (category 3 for IORT). For patients previously treated with EBRT at the recurrence site, recommended therapy for isolated relapse includes: 1) surgery with (or without) IORT (category 3 for IORT); and/or 2) systemic therapy with (or without) palliative RT.

Treatment of Recurrent or Metastatic Disease

The recurrence rate is high in uLMS (50%–70%). The guidelines provide recommendations based on tumor resectability and patients prior RT exposure. Treatment recommendations are made according to the site and nature of the recurrence.

Local recurrences are classified as recurrence in the vagina/pelvis with imaging that is negative for distant metastatic disease. Surgical and RT treatment pathways are provided. The surgical pathway for treating local recurrence in patients without prior RT exposure includes the option of IORT (category 3 for IORT). Preoperative EBRT and/or systemic therapy are also options to consider. For residual disease following surgery in patients without preoperative RT, EBRT with (or without) brachytherapy and/or systemic therapy can be considered. Primary RT offers an alternative pathway for treating localized recurrence in patients without prior exposure. EBRT should be given along with the option of brachytherapy and systemic therapy. For both the surgical and RT treatment pathways, further adjuvant systemic therapy should be considered after initial treatment.

Patients with local recurrence who have had prior RT exposure can be treated with: 1) surgery with the option of IORT and/or systemic therapy (category 3 for IORT); 2) systemic therapy; or 3) selected reirradiation with EBRT and/or brachytherapy.



C Current Practice

Practice consolidation

DISTRICT	INDICATION Stage/Locally advanced	INSTITUTION	RESULTS	REMARKS/IOeRT effects
ESOPHAGO-GASTRIC	Resectable	HGUGM (1)	5 y 85% LC	IOeRT significant improvement of LC
	Stage II and III	Meta-analysis HCMU (2)	IORT improved LC	Favourable effect of IORT in pts with stage II and III
GASTRIC	Resectable	Systematic review (3)	St III IOeRT promoted OS	Any stage IOeRT promoted local control
PROSTATE	Metastatic D1 and D2	Saitama Cancer C (4)	5-10 y 76/62% OS	In D2 IORT significantly cancer-specifIc survival
RENAL	Recurrent/Primary resectable	US-Europe Pooled-analysis (5)	5y 37% (p) VS 55% (r) OS	Survival affected by nodal involvement sercomatoid features and IORT dose
PEDIATRIC	Ewing/ Rhabdomyosarcoma	Pooled-European (6)	5-10 y 74%-68%OS	R1 and recurrent influence outcome
	Neuroblastoma + sarcoma incomplete resection	Heidelberg Univ (7)	1/18 local recurrences	6 clinicaI significant late toxicity
	Primary extremity soft-tìssue	Multicentric Pool ed Analysis (8)	10 y 85% LC, 76% DFS, 81% OS	IOeRT boost increased LC with low toxicity rates
OLIGO-RECURRENCES	Gynecologic, rectal	HGUGM (9)	5 y 53% LC, 46% OS	EBRT + IOeRT compensate adverse factors fragmentation
	STS, head and neck uterine, colorectal	Univ of Navarre (10)	5 y 31 % LRC, 57% DMFS, 31%0S	Gross macroscopic resection is significant for LRC and radiation dose for survival

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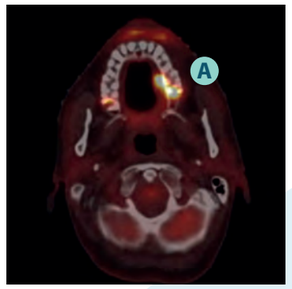
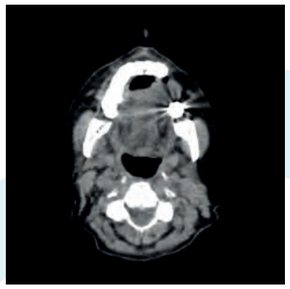
Extremity recurrent sarcomas: Sarcoma; 2015;91:3565

Legend

HCMU = Hospital of China Medical University
MCR = Mayo Clinic Rochester
LC = Local Control
LRC = Local Regional Control
OS = Overall Survival
DMFS = Disease Metastasis Free Survival
m = months
y = years
pts = patients
(p) = primary locally advanced disease
(r) = current disease
St = stage
IMRT = Intensity Modulated Radio Therapy
IOeRT = IntraOperative electron RadioTeraphy
R0 = complete remission
R1 = microscopic residual tumor
R2 = macroscopic residual tumor
C = Centre
S = Surgery
CT = Chemotherapy
CRT = Chemoradiotherapy
RT = Radiation Therapy
EBRT = External Beam Radiation Therapy
SR = Survival Rate
STS = Soft Tissue Sarcoma
D1 = cancer spread to the lymph nodes only
D2 = cancer spread to the distant lymph nodes and or bones or internal organs
HGUGM = Hospital General Universitario Gregorio Magno
cT2-4N+ = clinical stage transmural or metastatic nodes
pT4N0/T1-4N = locally advanced stage involving other organs/structures or metastatic pelvic nodes

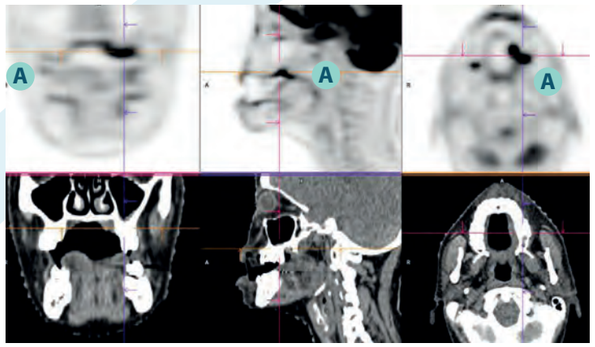
Indications **Cancer of the hard palate**

Patient 69 years old, female

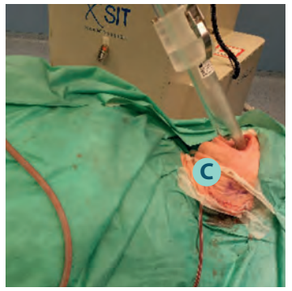
Chrono-description

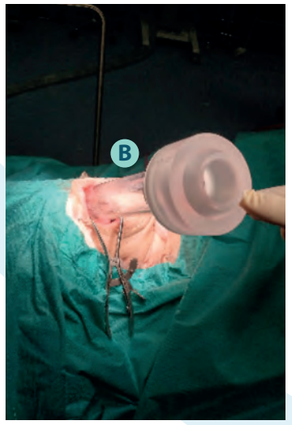
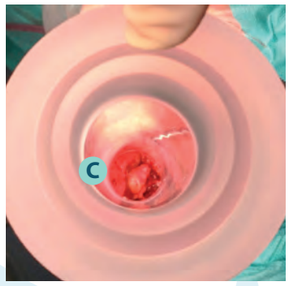
01.04.2019 Biopsy squamous cell carcinoma
Bone involvement
2 x 2cm lesion
9.5.2019 PET SUV 4,85 A



23.05.2019 Resection + **IOeRT** + neck nodal dissection

12 MeV
12.5 Gy
3 cm B
45° beveled
Tongue and lips displaced
C



Definitive pathology:
Squamous cell carcinoma with bone imvolvement
29 nodes free of metastases

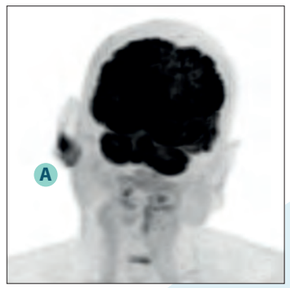
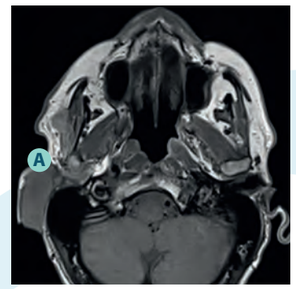
Postoperative radiotherapy
10 x 270 cGy VMAT

23.04.2021 Follow-up status:
Oro-nasal fistula (corrected)

11.11.2020 PET-CT:
no evidence of malignant disease

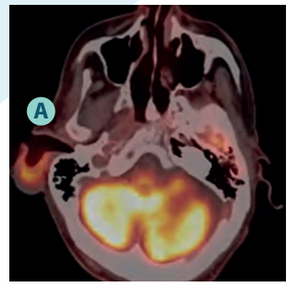
Indications **Recurrent skin cancer of the ear**

Patient 86 years old, male

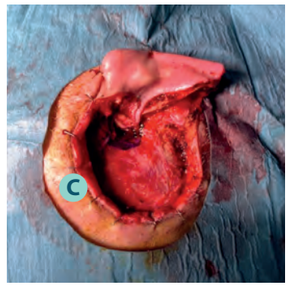
Chrono-description

21.12.2018 Cancer resection shoulder
9 x 7 cm lesion
Pathology: infiltrative solid basocelular carcinoma



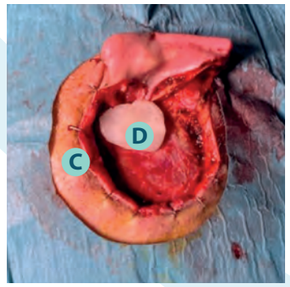
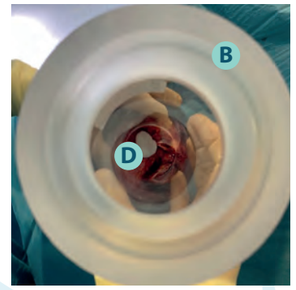
19.02.2019 Cancer resection peri-auricular lesion A

Pathology: squamous cell carcinoma 4 x 5 x 2 cm
Involved marging at the cartilagle edge
16 nodes free of metastases




19.02.2019 Resection + **IOeRT** + flap reconstruction

12 MeV
20 Gy
bolus 0.5 cm
7 cm B
15° beveled
Skin borders displaced C
Bolus at external ear canal
D

23.04.2021 Follow-up status:
no evidence of malignant disease

Indications **Recurrent melanoma of the plantar foot**

Patient 57 years old, male

Chrono-description

29.04.20 Cancer resection

Pathology: desmoplastic melanoma

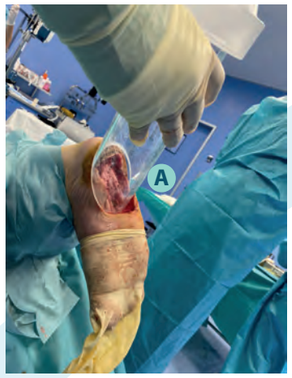
Immunohistochemistry: S100 + SDX-10 + Ki67 10 %

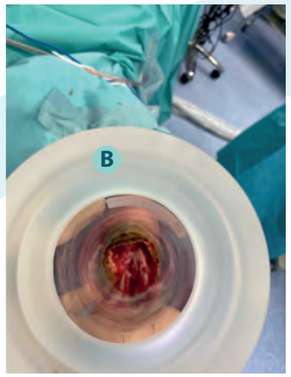
13.05.20
19.06 20
29.07.20
03.09.20 Medical examination: pathology proven recurrent melanoma

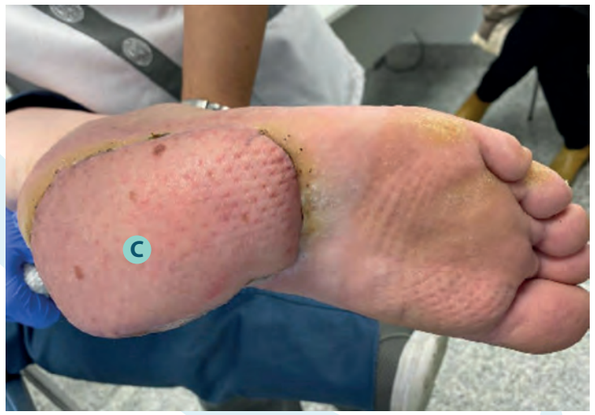
29.01.21 Resection A + **IOeRT** + flap reconstruction B

12 MeV
20 Gy
bolus 0.5 cm
7 cm C
45° beveled
Skin borders displaced

23.04.2021 Follow-up status: no evidence of malignant melanoma







C Current Practice
Practice consolidation
Selected cases

Indications **Recurrent skin cancer of the nose**

Patient 72 years old, female

Chrono-description

16.07.2019 Cancer resection nasal lesion A

Pathology: squamous cell carcinoma margin involved

21.08.2019 Cancer resection
Pathology: squamous cell carcinoma margin involved

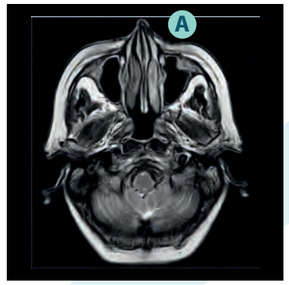
6.11.2019 Cancer resection marging involved

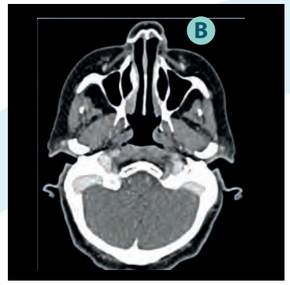
19.11.2019 Re-resection + **IOeRT** + reconstruction B

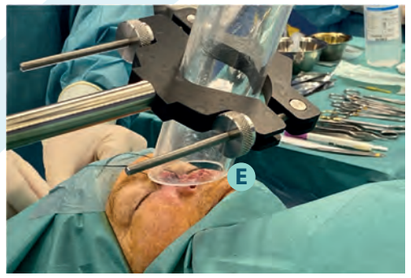
Field-within-a-field C
12 MeV + 10 MeV
10 Gy + 5 Gy
bolus 0.5 cm D
7 cm + 3 cm E
30° + 15° beveled

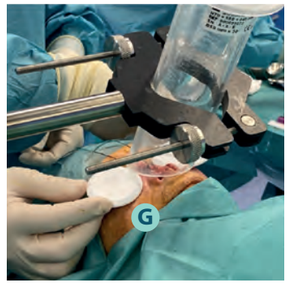
Skin borders displaced F
Eyes protected G

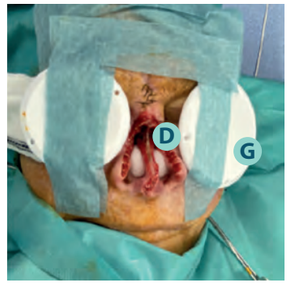
23.04.2021 Follow-up status: torpid reconstruction evolution, no evidence of malignant disease

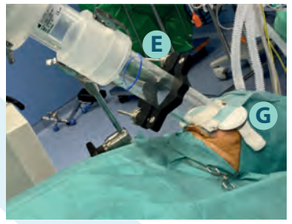


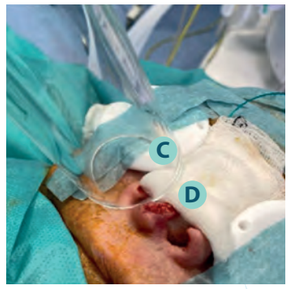












Indications **Recurrent adenocarcinoma of the lung**

Patient 62 years old, female

Chrono-description

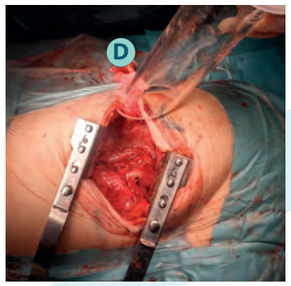
03.07.2013 Lobectomy pT1cN0M0
Carbo + Taxol x 6 cycles

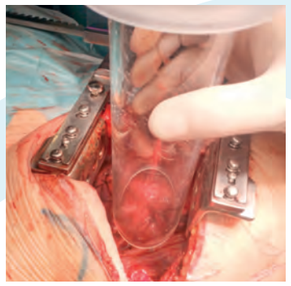
30.11.2018 Oligo-recurrence
Biopsy proven
PET SUV 4,5 A

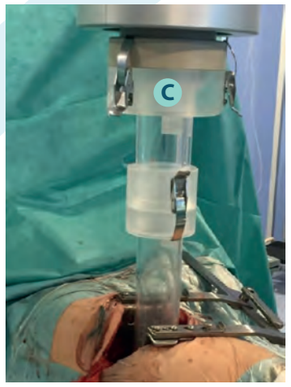
07.02.2019 Resection + **IOeRT** + flap coverage B
8 MeV
10 Gy
5 cm C
45° beveled D
Lung parenchyma displaced E

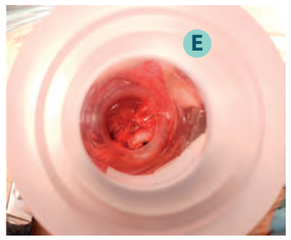
Postoperative radiotherapy
10 x 270 cGy VMAT

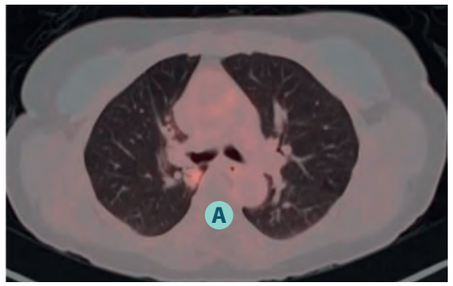
23.04.2021 Follow-up status:
no evidence of malignant disease

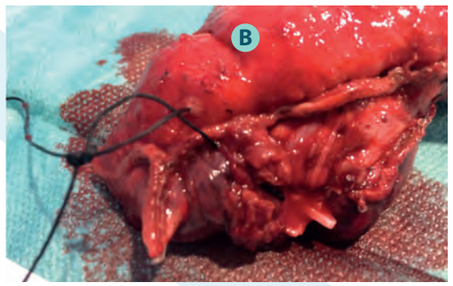












Indications **Nodal oligo-recurrence prostate cancer**

Patient 71 years old, male

Chrono-description

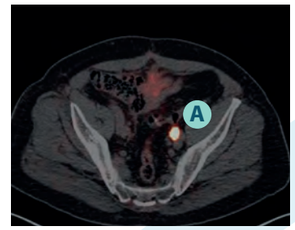
18.01.2011 Radical prostatectomy (PSA 10)
Gleason 4 + 3, 20% specimen,
Extracapsular extention, perineural invasion

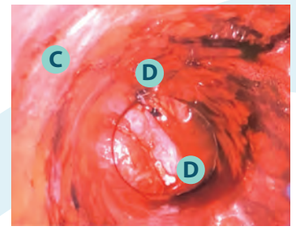
08.03.2016 Biochemical progression (PSA 0,79)
Pelvic radiotherapy

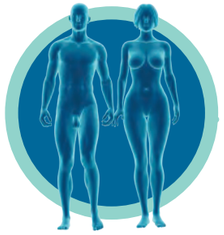
17.10.2019 PSA 4.86
PET-PSMA positive
Solitary nodal recurrence A

02.03.2020 Robotic surgery Da Vinci guided + **IOeRT** B
3 cm specimen
extracapsular extension
adenocarcinoma gleason 4 + 4 pN1
12 MeV
15 Gy
3 cm
45° beveled
Small bowell, bladder, ureter displaced C
Upper and lower limits marked by fiducials D

23.4.2021 Follow-up status:
PSA 0.01
no evidence of malignant disease







C Current Practice

Practice consolidation

Selected cases

Indications **Primary retroperitoneal sarcoma**

Patient 63 years old, female

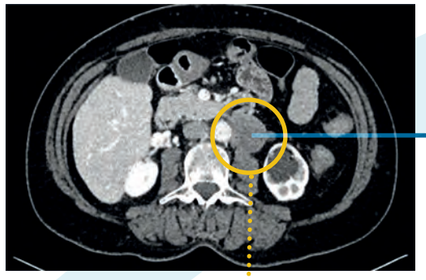
Chrono-description

02.08.2018 Resection + **IOeRT**
Margin involved (A)

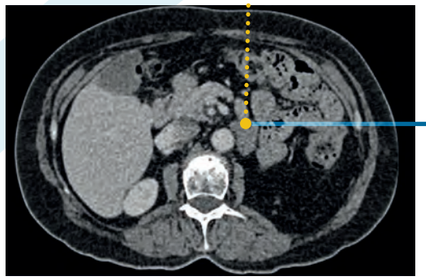
IOeRT
Field-with-in-a-field technique
5cm/15° beveled (B)
+ 10 cm/30° beveled (C)
12 MeV/12.5 Gy
+ 10 MeV/5Gy

25.09.2018 - 30.10.2018
Post-operative external beam radiotherapy 45 Gy
Follow-up

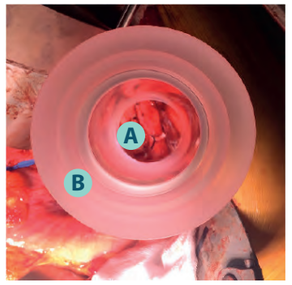
06.05.2021 No evidence of disease

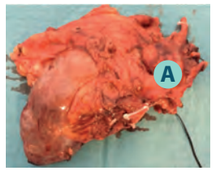


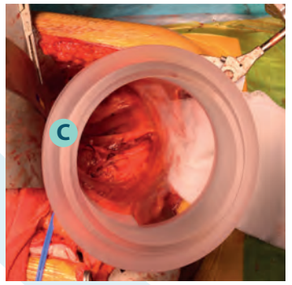
Initial sarcoma

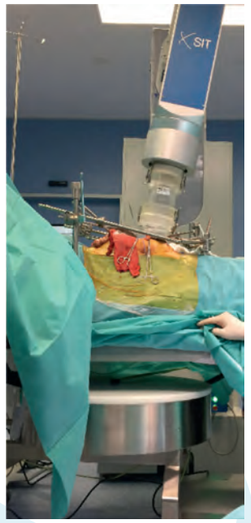


Local control at 30 months









C Current Practice

Practice consolidation

Selected cases

Indications **Nodal recurrence of gastric adenocarcinoma**

Patient 72 years old, male

Chrono-description

4.11.2016 Total gastrectomy
pT3N0Mx adenocarcinom

10.01.2018 Solitary nodal recurrence
Inoperable portal vein invasion (A)
Biliary stent FOLFOX
7 cycles (intolerance neuropathy)

09.01.2020 Oligo-progression

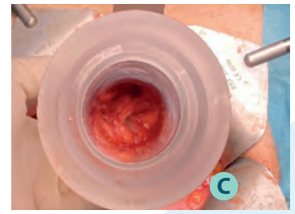
19.01.2020 Preoperative radiotherapy
50 Gy VMAT
COVID19

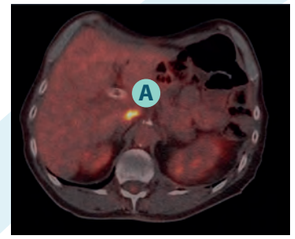
22.05.2020 Laparotomy + tumor exposure + **IOeRT**
ultrasound guided (B)
12 MeV
15 Gy
5 cm
30° beveled
Colon + duodenum + liver displaced (C)

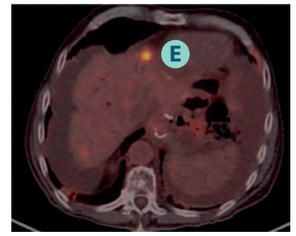
14.09.2020 Progression para-aortic nodes (proton therapy) (D)

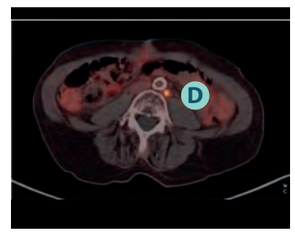
13.02.2021 Liver metastases (E)

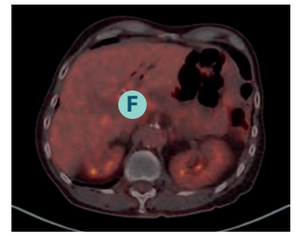
23.04.2021 Follow-up status:
Alive with disease (control in IOeRT nodal region) (F)

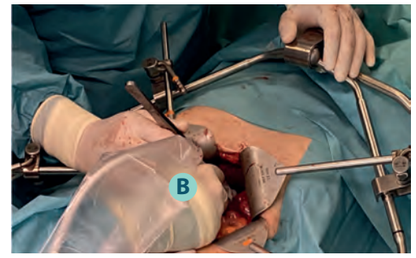


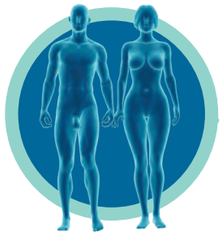












C Current Practice

Practice consolidation

Selected cases

Indications **Recurrent adenocarcinoma of the pancreas**

Patient 45 years old, female

Chrono-description

20.01.2019 Unresectable 39 x 25 mm adenocarcinoma

FOLFIRINOX x 6 cycles

17.06.2019 Radiotherapy 50.4 Gy + Capecitabine (A)

30.11.2018 Oligo-persistance

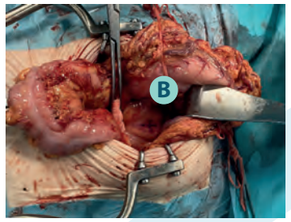
PET SUV 3.67

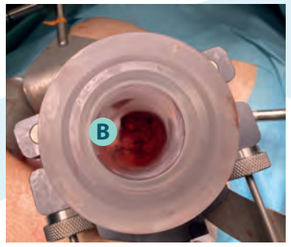
07.02.2019 Laparotomy + tumor exposure (B) + + ultrasound-guided **IOeRT** (C)

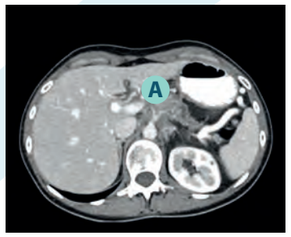
8 MeV
20 Gy
5 cm
15° beveled

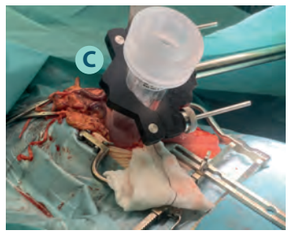
Stomach + colon + duodenum displaced

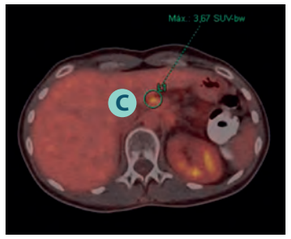
23.04.2021 Follow-up status: (D)
CA19.9 increased >300
PET stable
Asymptomatic

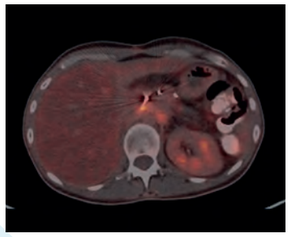












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