

# VIII CONGRESO ALATRO

Asociación Ibero Latinoamericana  
de Terapia Radiante Oncológica

LIMA - PERÚ

Congreso ALATRO 2022

16 - 18 de Noviembre de 2022



Incrementando la calidad de  
vida con RIO para tumores  
cerebrales y otras partes del  
cuerpo

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Brazil



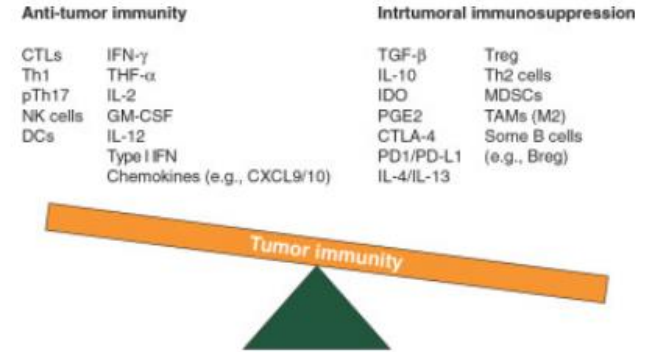
# DISCLOSURE

- I have travel allowance from Zeiss
- This deck was prepared by me and reflects my own opinions and not necessarily those of AC Camargo Cancer Center or Zeiss.



# Immune Tumor Microenvironment

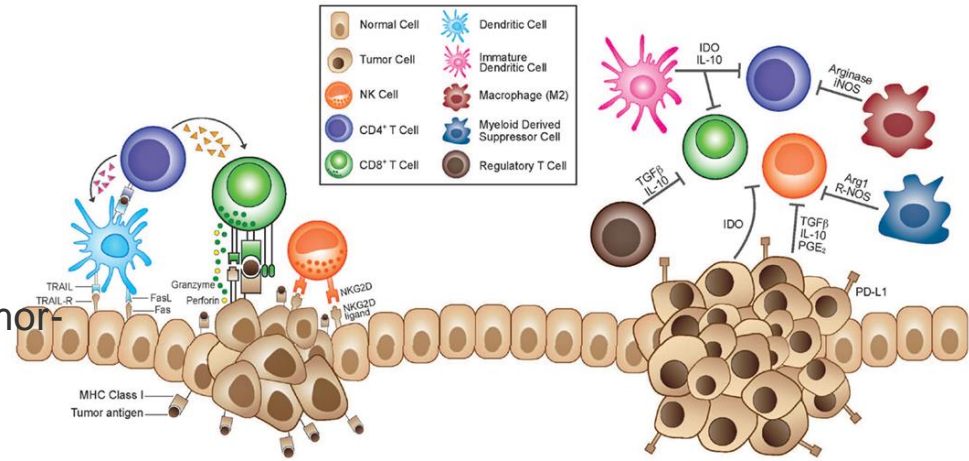
- **comprises**
  - extracellular matrix
  - stromal cells
  - immune cells
    - cytokines
    - metabolites



*Balachandran et al.  
Nature. 2017;551(7681):512-516.  
Ott et al.  
J Clin Oncol. 2019;37(4):318-327.*

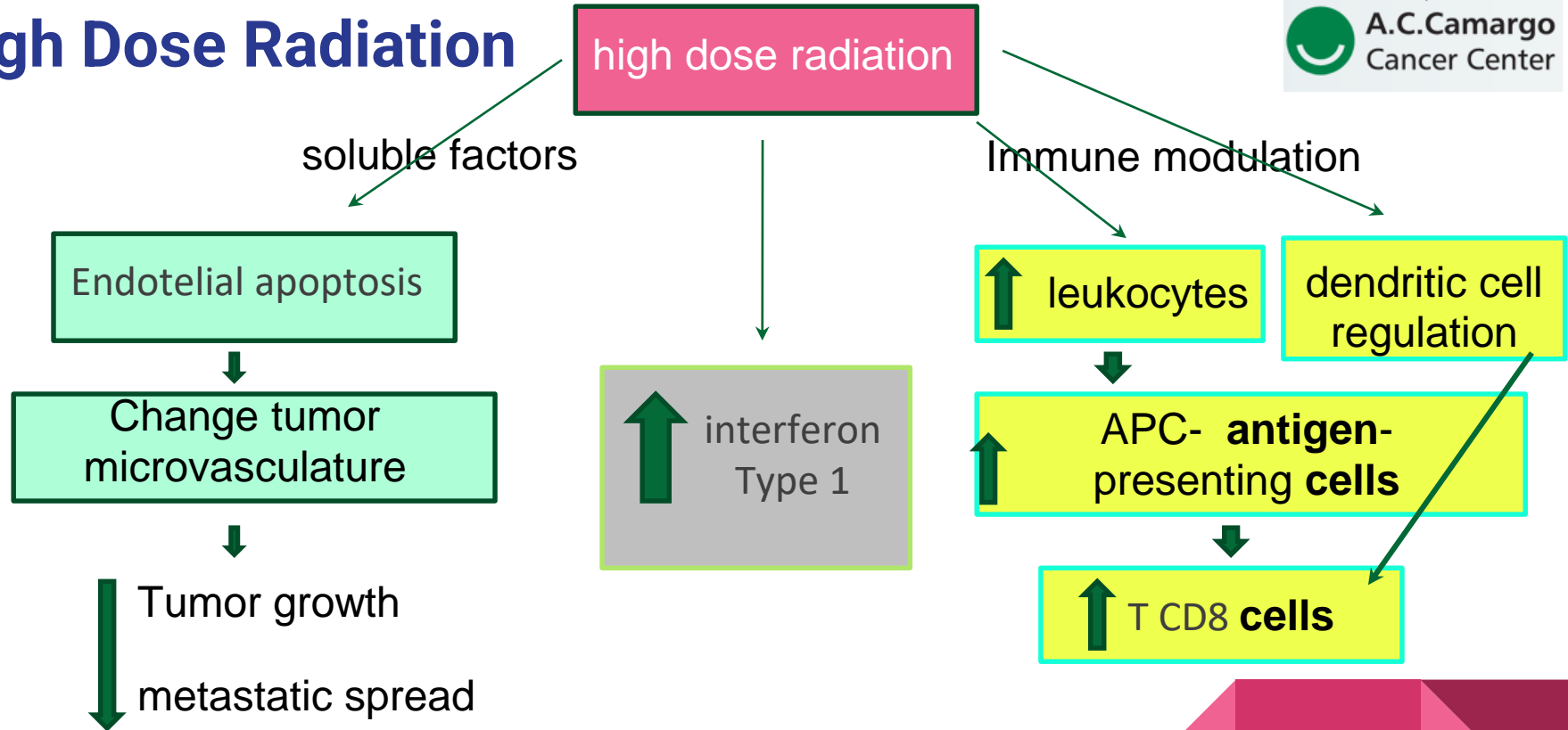
# Immune Tumor Microenvironment → immunosuppressive

- **impenetrable network**
  - limited infiltration of CD8<sup>+</sup> T cells
  - resistance to most single-agent therapeutic approaches
- **antagonizes host anticancer immunity**
  - myeloid-derived suppressor cells, tumor-associated macrophages,
  - tumor-associated neutrophils, and regulatory T cells.
- **promotes carcinogenesis**





# High Dose Radiation



# LINACs & Intraoperative radiation therapy systems



# SURGERY

Timing

2-8h00

IORT

1h00

End of Surgery

1-6h00

OAR  
@  
RadOnc Dept.



RadOnc Team  
locate the E<sup>-</sup>  
applicators



Stop LINAC



Transfer patient  
to  
LINAC  
+  
Treatment



Patient  
transferred  
back to  
OAR



Figura 1 – Corredor e Sala Cirúrgica do setor de Radioterapia (1º subsolo)

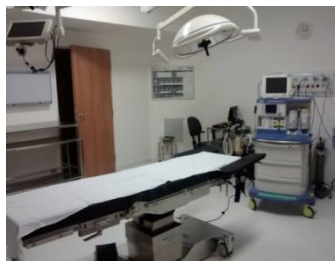


Figura 2 – Interior da sala cirúrgica do setor de Radioterapia



Figura 3 – Corredor e 2 salas de aceleradores lineares



Figura 4 – Corredor interno da sala do acelerador



Figura 5 – Interior da sala do acelerador

# Advantages low energy X-Rays

## Local & Immunological

- No major radiological protection needed
- Operating Rooms
- X-Rays interactions

→ Photoelectric  
&

→ Coulomb scattering

- Activation
  - T lymphocytes
  - APC (antigen-presenting cells)



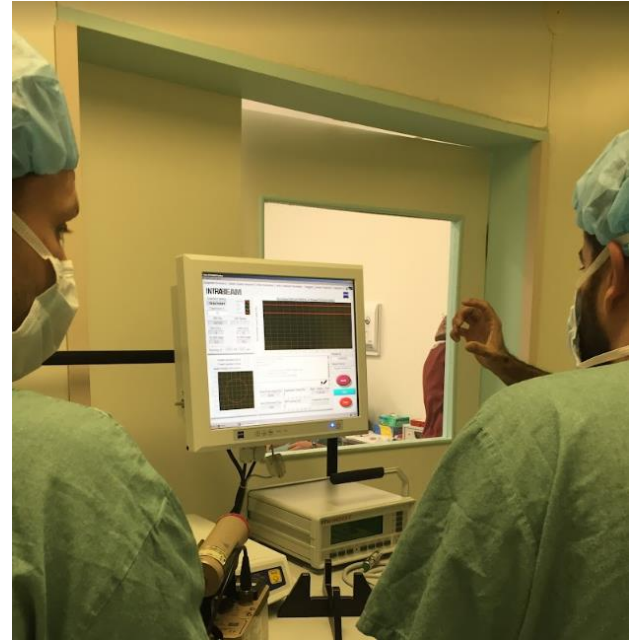
*Tandl et al.  
J Gen Physiol*

(2022) 154 (5): e202112865.



# Objectives of IORT

- **Primary**
  - local control (LC)
  - QOL
- **Secondary**
  - overall survival (OS)
  - Improved QOL



## Other areas besides breast...



# PANCREATIC ADENOCARCINOMAS

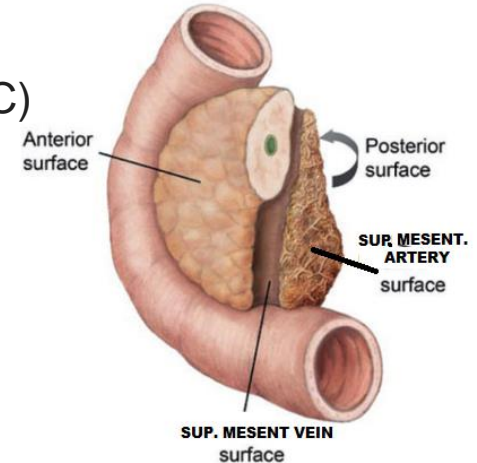
- 2021→ 60, 430 new diagnoses in the US.
- incidence is increasing by 0.5% to 1.0% per year
- projected
  - second-leading cause of cancer-related mortality by 2030.



The 5-y survival rate:  
approached 10% for the first time in 2020,  
compared with 5.26% in 2000.

# Background

- Borderline / locally advanced pancreatic adenocarcinoma (LAPAC)
  - recommend neoadjuvant chemotherapy
    - FOLFIRINOX
      - (folinic acid, fluorouracil, irinotecan and oxaliplatin)



—> ***addition intraoperative radiation therapy (IORT)***

**AS** microscopically positive margins (R1) negatively impact survival

- more effective treatment
- improved survival rates

# Methods and Patients

- uni-institutional study
  - Borderline / locally advanced pancreatic adenocarcinoma (LAPAC)

## Data collection

- AC Camargo Cancer Center
- May 2019 to October 2021

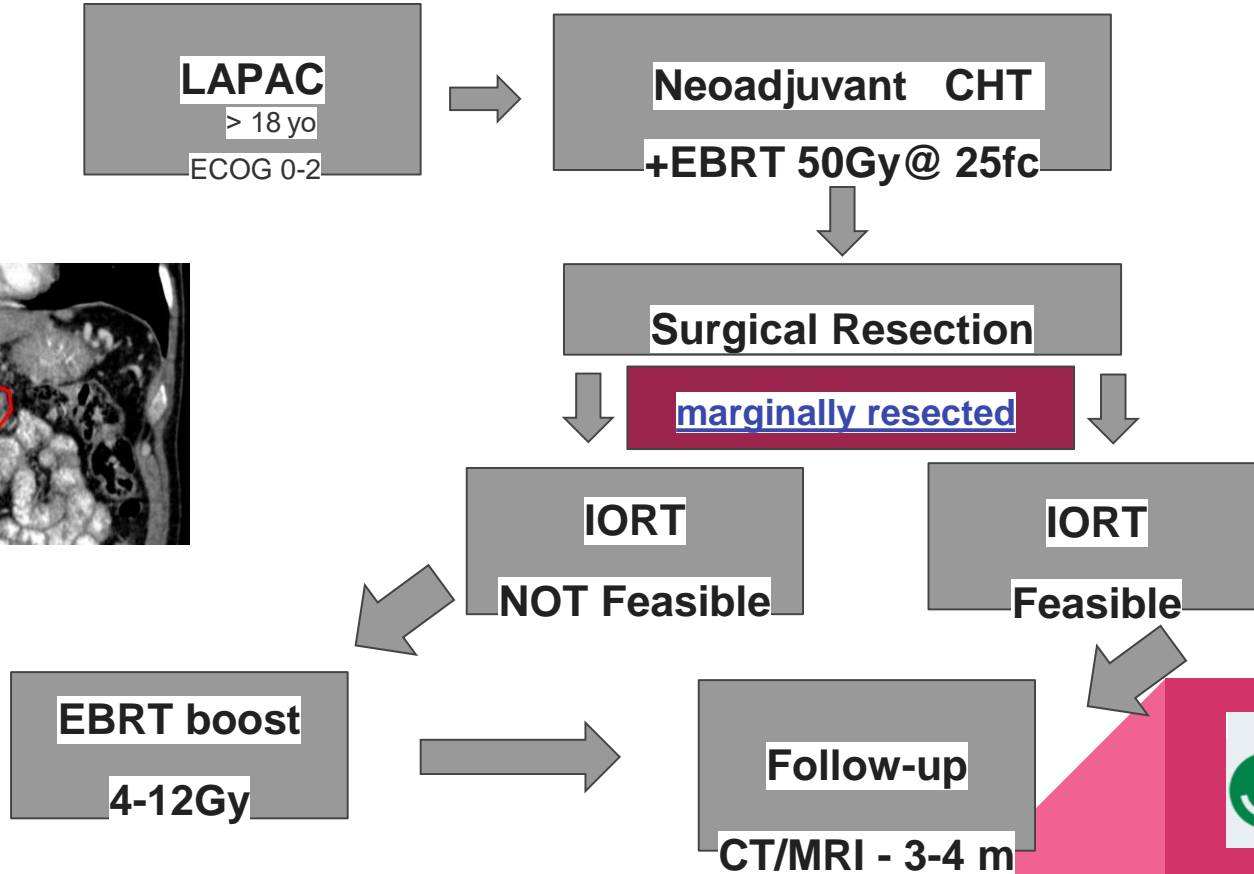
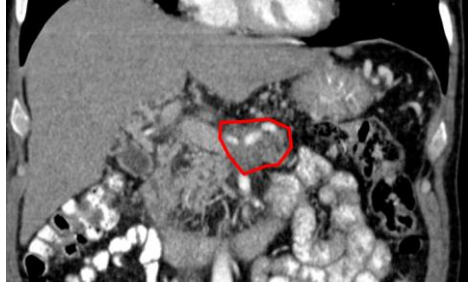


## Inclusion criteria - uni-institutional study

- 18 years of age or older
- Histologically confirmed adenocarcinoma of the pancreas
- Eastern Cooperative Oncology Group –PS -0–2
- Stage I–III disease
- Resectable disease &
  - Absence of distant metastases
  - *marginally resected expected planes* around :
    - i. the celiac axis, hepatic artery, and superior mesenteric artery
    - ii. Absence of direct involvement of inferior vena cava or aorta
- Adequate bone marrow function
- Adequate renal function
- Written informed consent



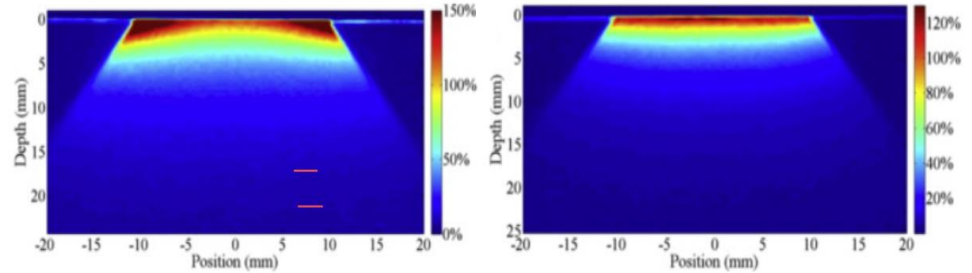
# TREATMENT



# RESULTS

## Three patients treated

- Doses prescribed
  - @ surface of flat or surface applicators
    - 12 Gy in 2
    - 15 Gy in 1
- Median follow-up → 22 months
- all patients → LC - 100% OS
- Two patients are alive with no evidence of disease
- One patient had LC → progression 8 months after IORT (pancreatic tail)
- Severe adverse events (grade 3 and 4) were not observed.



*Unpublished data*



# Discussion - LAPAC

Spherical, flat and surface applicators

→ suitable to be accommodated in the tumor bed

Large dose to the tumor bed with rapid dose fall-off

- reduced dose to OARs
- eliminate the re-population of residual tumor cells
- increases local control



*Unpublished data*

# CONCLUSION

LAPAC treated with IORT

- few adverse events
- less treatment time



→ IORT may mitigate the adverse effect of an R1 resection, with advantages in LC → OS

→ Immunologic aspects of low energy X-Rays interactions shall be a field of future research

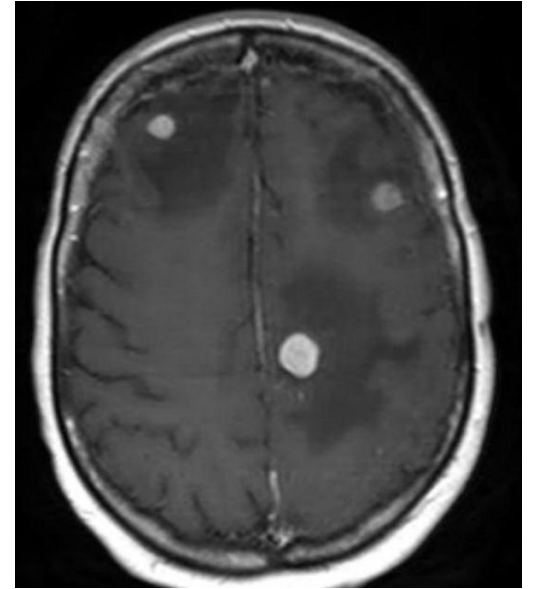
*Unpublished data*

# Brain Mets

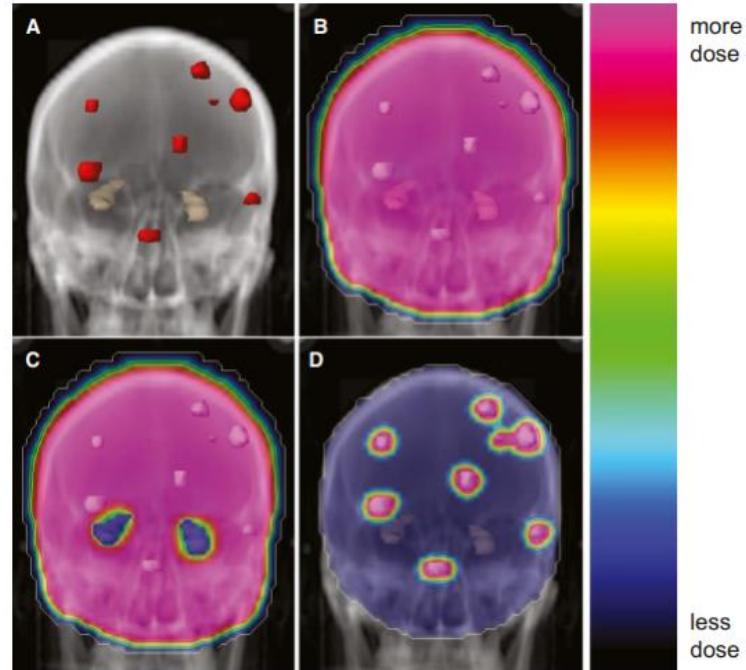
- 20-40% of patients with cancer -> RT
- ~ 300.000 patients each year with BM in USA
- Breast, Lung and Melanoma: 80% of cases

## Current therapies include:

Stereotactic radiosurgery, whole-brain radiation therapy, surgical resection, laser-interstitial thermal therapy, systemic cytotoxic chemotherapy, targeted agents, and immune-checkpoint inhibitors.



# Whole-Brain RT x Stereotactic Focal RT



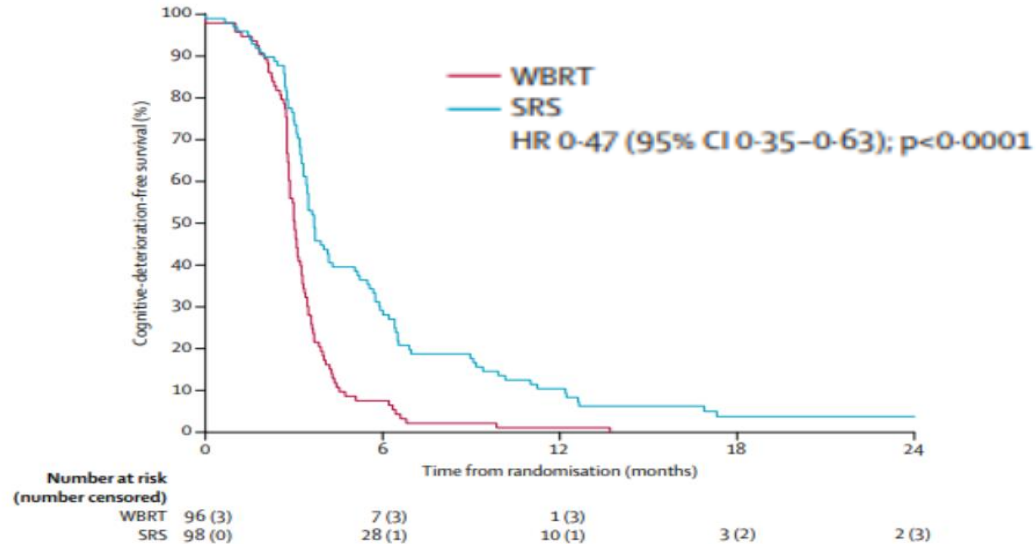
# AND AFTER SURGICAL RESECTION OF BMs???



**NCTG N107C/CEC-3**  
Multicentre Phase 3 rand Trial

# PO-Rcir vs WBRT

**NCTG N107C/CEC-3**  
Multicentre Phase 3 rand Trial



**Cognitive  
Impact**



*Brown PD et al.  
Lancet Oncol 2017;18:1049-60*

# Whole-Brain RT x Stereotactic Focal RT

**Cognitive  
Impact**

**Brain Disease  
Control**

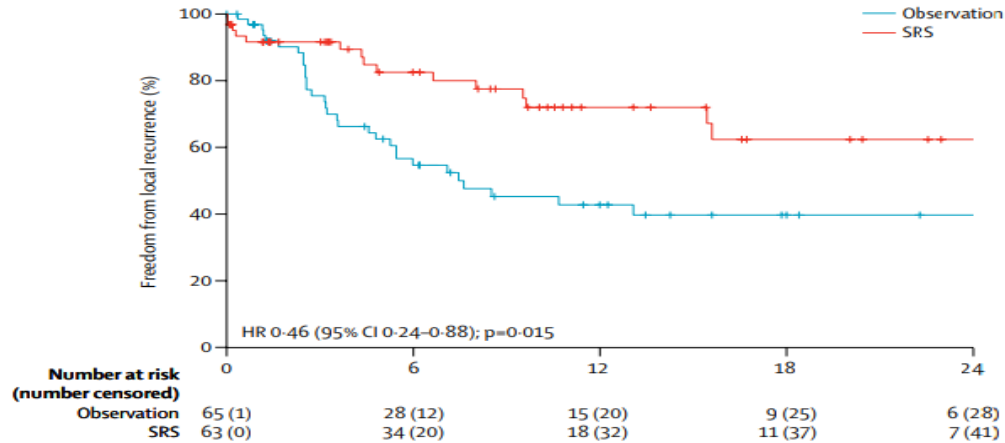


No difference in OS  
**Strategy → postpone WBRT**

*Moravan MJ et al.  
Cancer 2020;126:1390-406*

# PO-Rcir vs Obs

Single Center Phase 3  
rand Trial



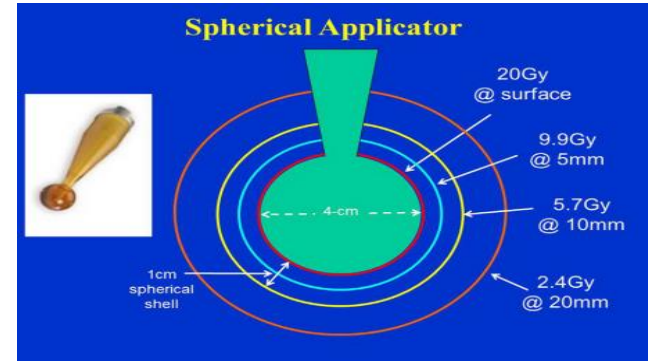
**Local  
Control**



# IORT for Brain Metastases

## Potential advantages of IORT for BM

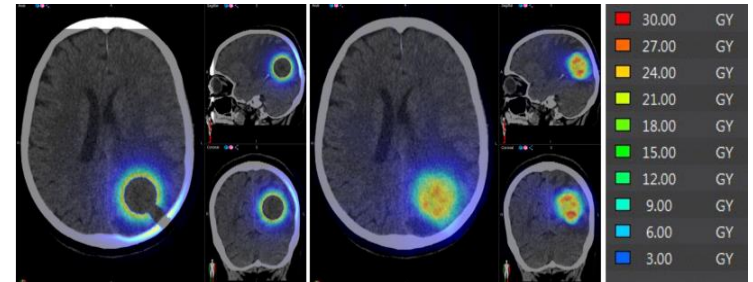
- Target-volume definition
- Steep dose fall-off
- Convenience and less delay in systemic therapy



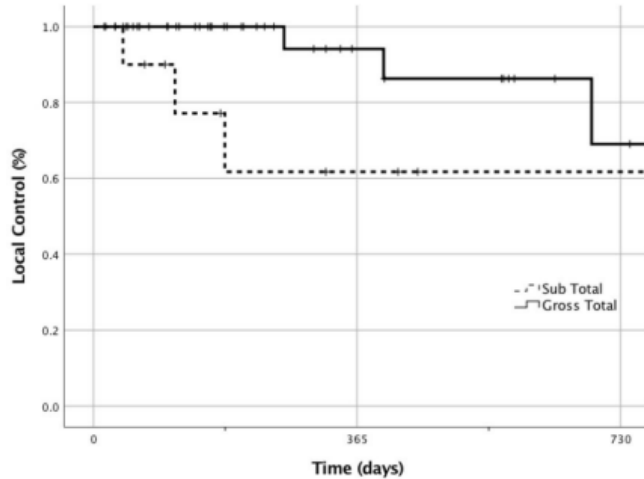
# IORT for Brain Metastases

**Intraoperative radiotherapy (IORT) for surgically resected brain metastases: outcome analysis of an international cooperative study**

- 54 patients from centers in Germany and USA
- IORT with Intrabeam → Dose: 18-30 Gy @ surface
- ~ FUp: 7.2 months
- ~ age - 64 yo



# IORT for Brain Metastases



N at Risk: GTR 44 24 12 10 4  
N at Risk: STR 10 3 5 1 1

Median follow-up - 7.2 months

LC



**Extent of Resection**

**Gross Total 94 %**

**vs**

**Subtotal - 62%**

**p = 0 .049**

# IORT for Brain Metastases: Final First-Stage Results of a Single-Arm, Open Label, Phase 2 Trial

## Investigator-initiated research

- Partially funded by Carl Zeiss Meditec AG
- *ClinicalTrials: NCT03789149*



## Endpoints

- Primary: Local Control (LC) and Distant Brain Failure (DBF) → death as a competing risk
- Secondary: Overall Survival (OS) and Radiation Necrosis (RN)

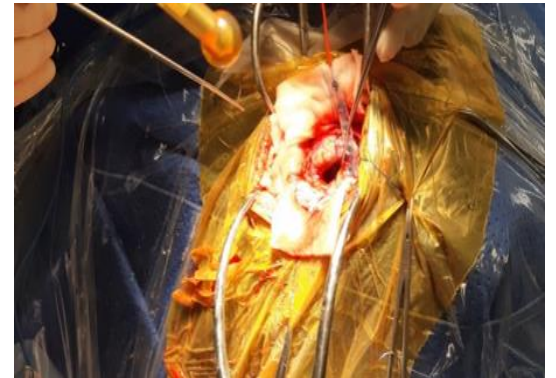
*in press*

# IORT for Brain Metastases: Final First-Stage Results of a Single-Arm, Open Label, Phase 2 Trial



## Methods

- Complete resection with histological confirmation BM
- Suitable for IORT with Intrabeam
- Dose prescription:
  - 18 Gy @ 1 mm of surface of spherical applicator



*in press*

# IORT for Brain Metastases: Final First-Stage Results of a Single-Arm, Open Label, Phase 2 Trial



## Results

- 12 patients screened and 10 accrued between June 2019 and November 2020

*in press*

# IORT for Brain Metastases: Final First-Stage Results of a Single-Arm, Open Label, Phase 2 Trial

## Results

- The median OS → not reached  
→ but estimated OS @ 6 and 12 months:  
80%
- 3 (three) deaths  
→ due to extracranial metastases

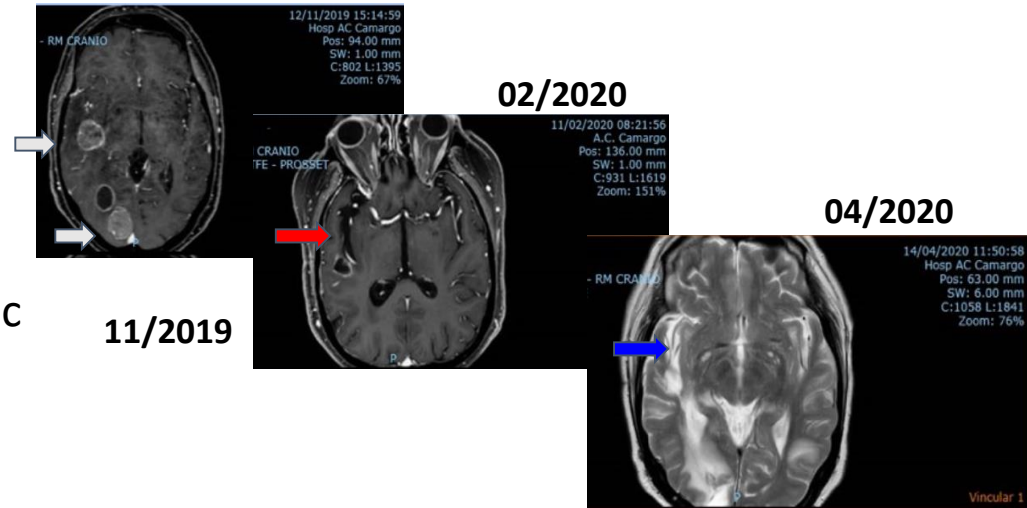
*in press*

# IORT for Brain Metastases: Final First-Stage Results of a Single-Arm, Open Label, Phase 2 Trial

## Complications

→ 1 (one) patient with asymptomatic RN @10 months after IORT

→ No patients with wound dehiscence



*in press*



# Head & Neck

## Salvage

→ local control (LC) is a critical element of the overall treatment

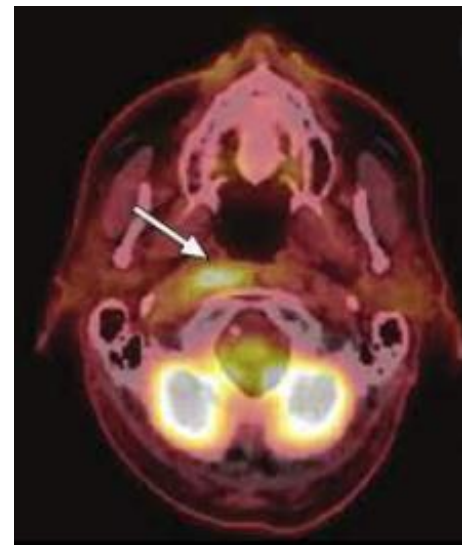
→ limited doses to OARs

→ Difficult to locate electrons cones

→ Lack of

– OARs @ RadOnc Depts

– Anesthetic transfers



# Re-irradiation

- **Technical Resources**

needed x available

- **Previous treatment**

dose

x

fractionation

x

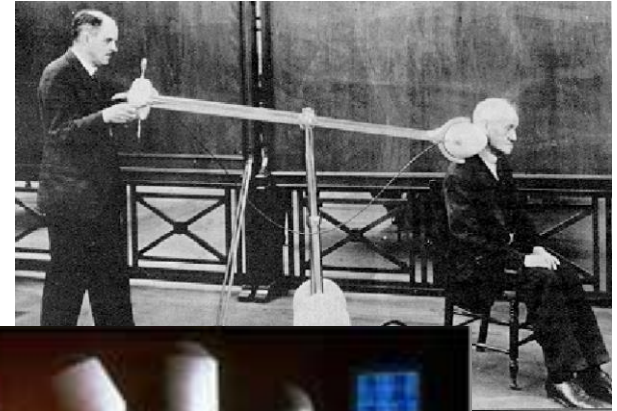
technique

x

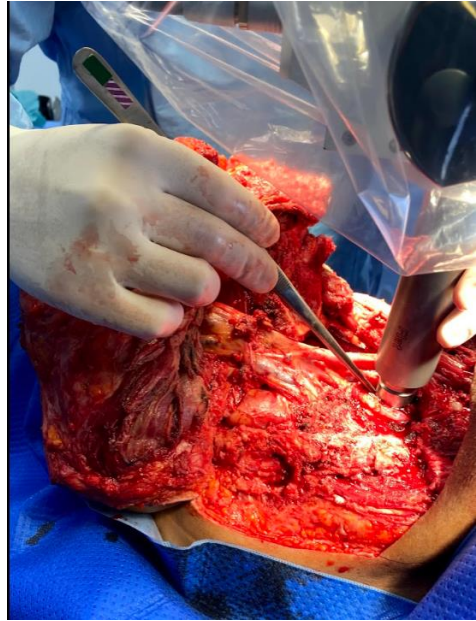
OAR

- **Associated comorbidities**

- **Estimated survival**



# Head & Neck



*unpublished data*

# Head & Neck

## Results

- 6 patients treated
  - LC 83.3% (5/6)
  - Deaths 66.6% (4/6) median OS 9 m
  - Deaths due to extracranial metastases 75% (3/4)



*unpublished data*

# Messages to take home

- Indications for IORT are evolving
- The link between high dose radiation and immune stimulation are still under evaluation, but there are many potential benefits
- Increased LC can positively reflect in OS
- Re-irradiation with IORT seems to be safer than other techs
- QOL can be improved by IORT



WE OFFER BETTER



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