OligoMetastatic Disease

B-STRO 2025

Charlien Berghen, UZLeuven

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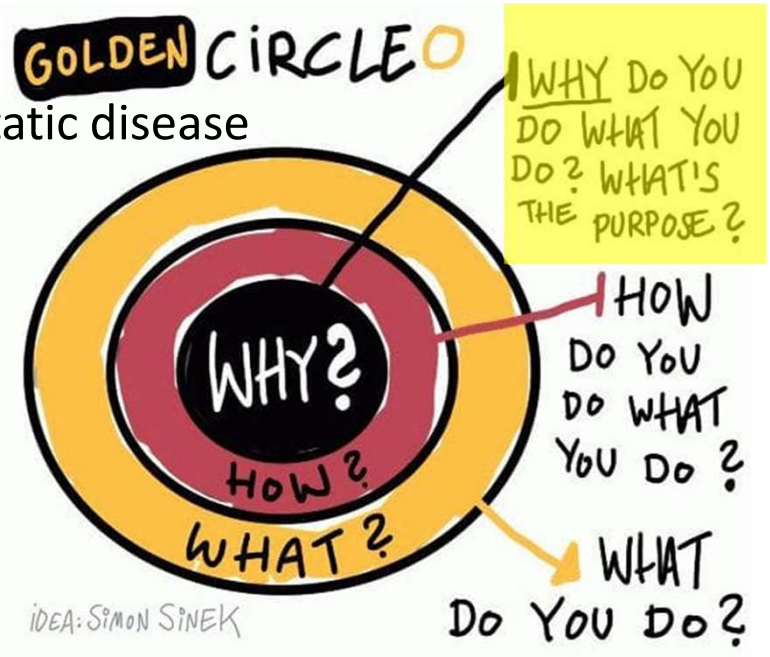
Oligometastatic disease



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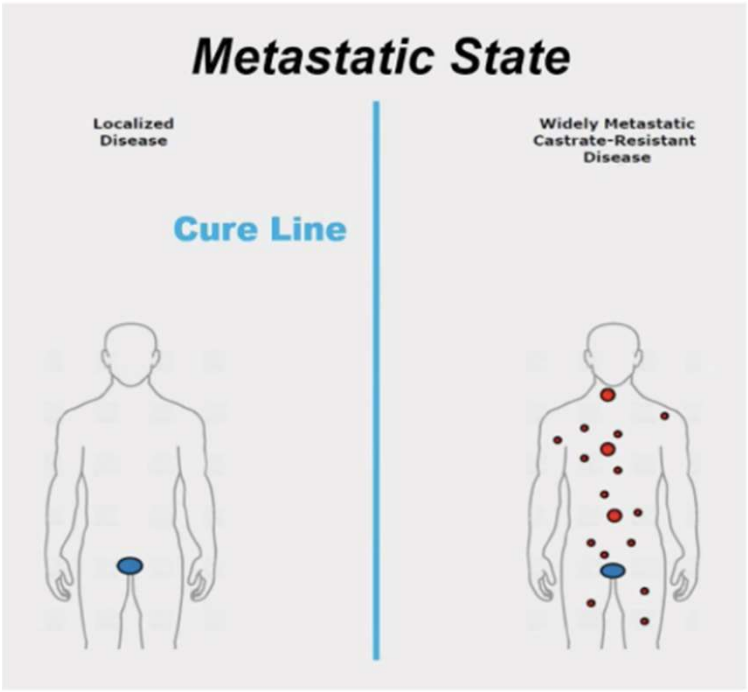

Tran et al 2017 JOP

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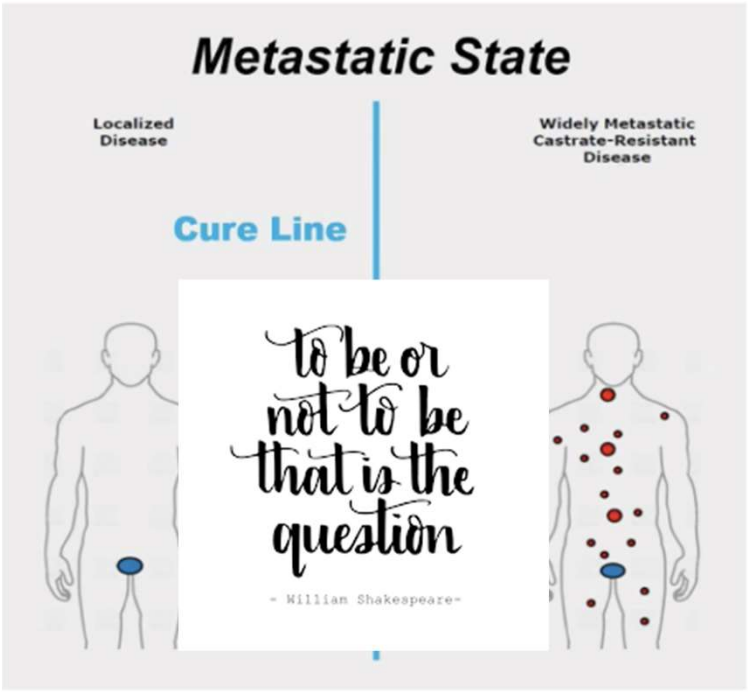

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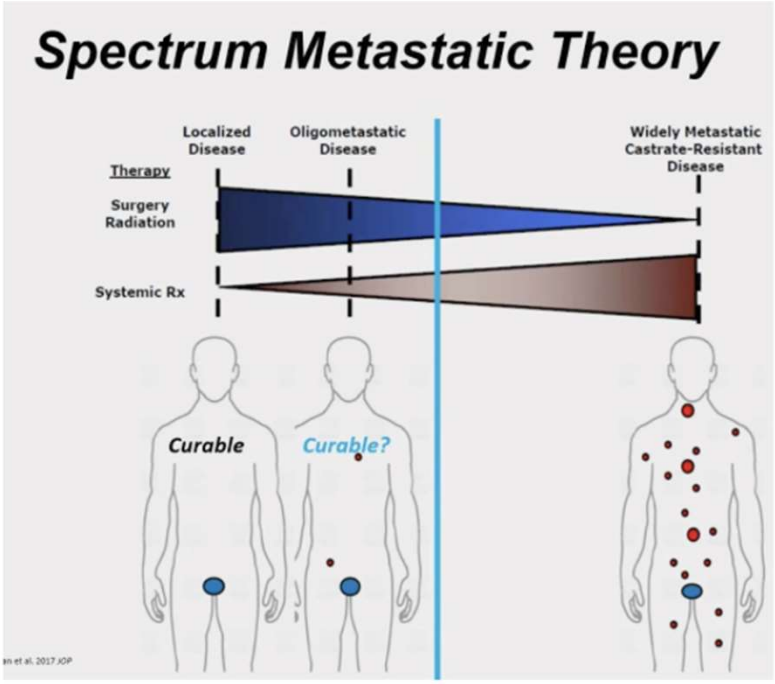

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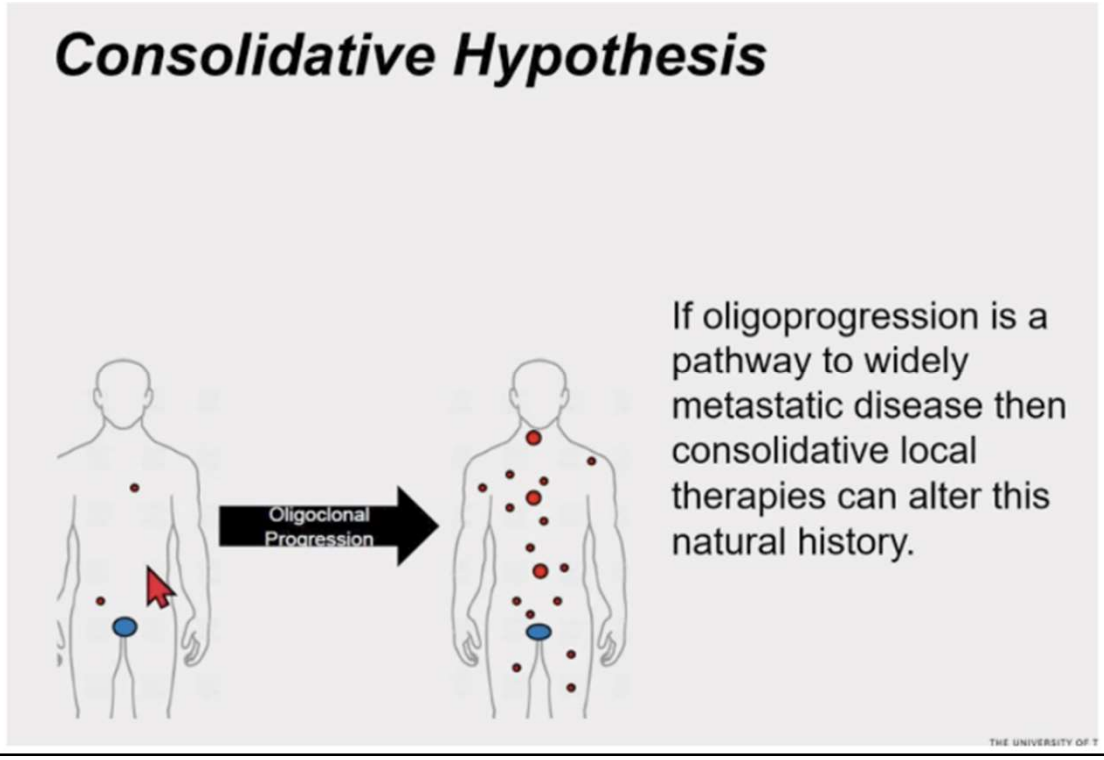

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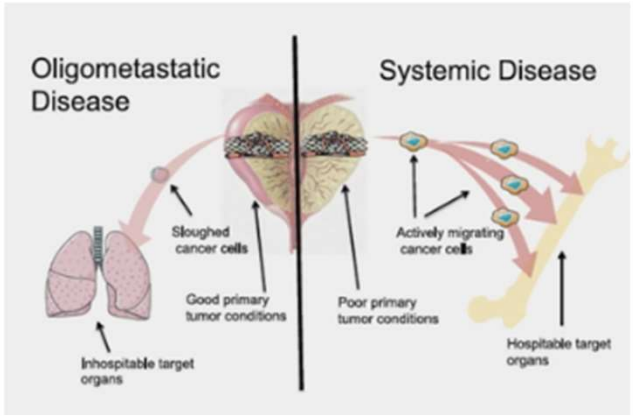

	Oligometastatic disease	Systemic disease
Primary tumour	Favourable microenvironment	Poor conditions creating undifferentiated aggressive clones
Sead (migrating cells)	Sloughed cancer cells	Actively migrating cells
Soils (target organs)	Inhospitable target organs (trap)	Hospitable target organs

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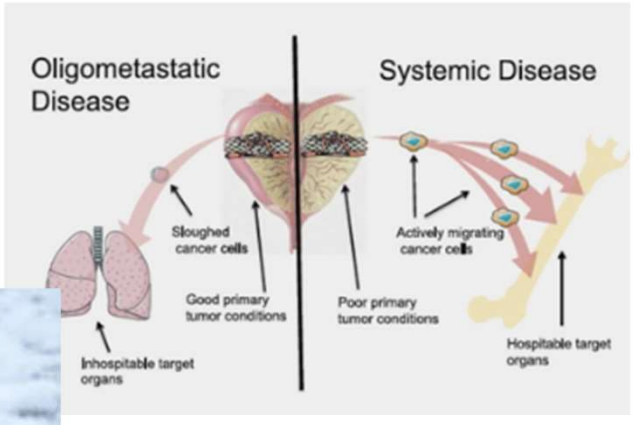

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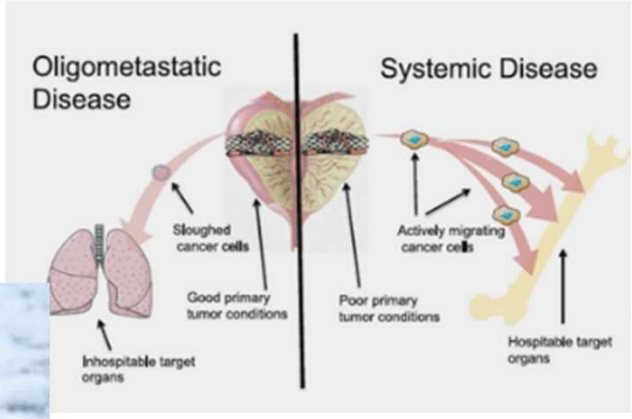

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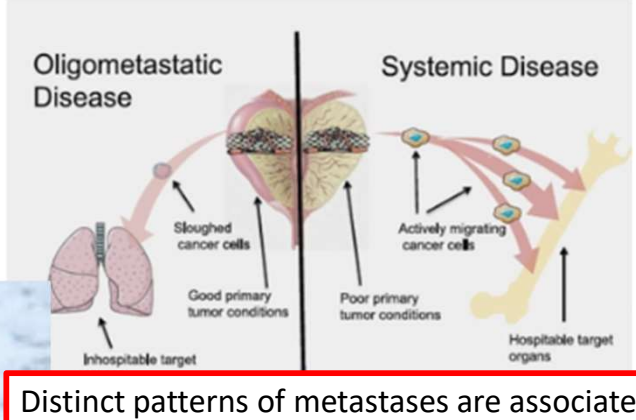

Distinct patterns of metastases are associated with some molecular signatures

	disease	
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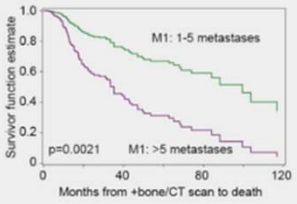
Evidence of an Oligometastatic Disease State:



Sridharan et al. Oligometastatic bone disease in prostate cancer patients treated on the TROG 03.04 RADAR trial

De novo prostate cancer
Garraway et al. Unpublished. VA Greater LA.

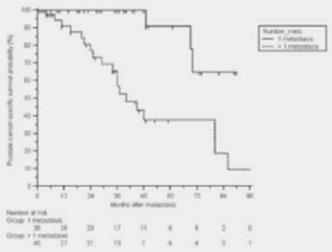


Fig. 4. Prostate cancer-specific survival following diagnosis of metastatic disease stratified according to the number of metastases (I vs. >I).

Ost et al , Prognostic Factors Influencing Survival In Non-Castrate Patients with Metastatic PC

BUT DO THESE DATA PROVE THAT OLIGOMETASTASIS IS A UNIQUE DISEASE STATE or JUST a FUNCTION OF TIME?

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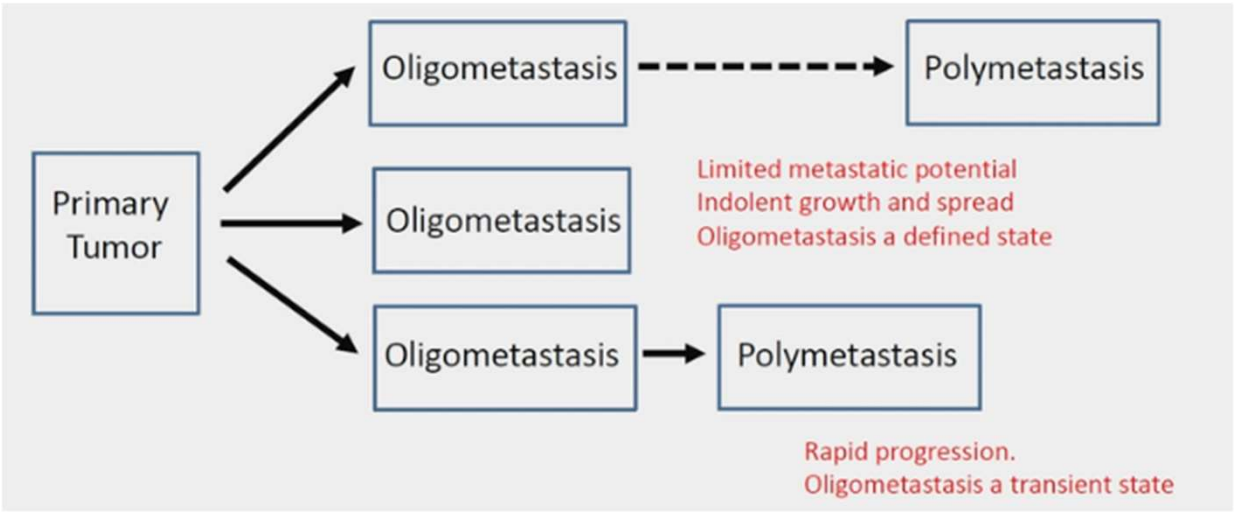

Yazid Belkacemi, MD, PhD
Nicolas Penel, MD, PhD ESMO PRO/ONCOL

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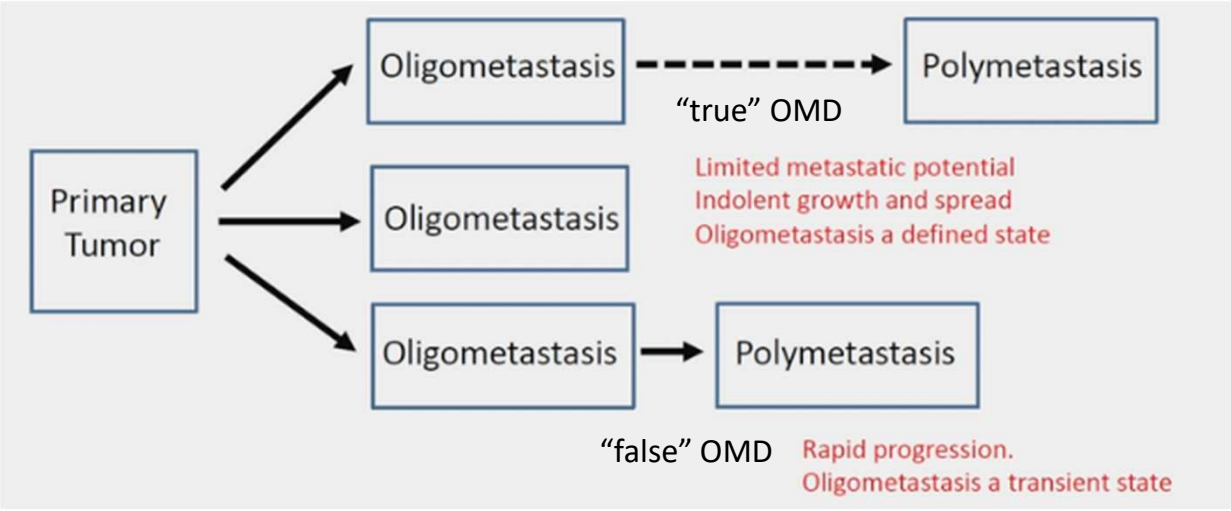

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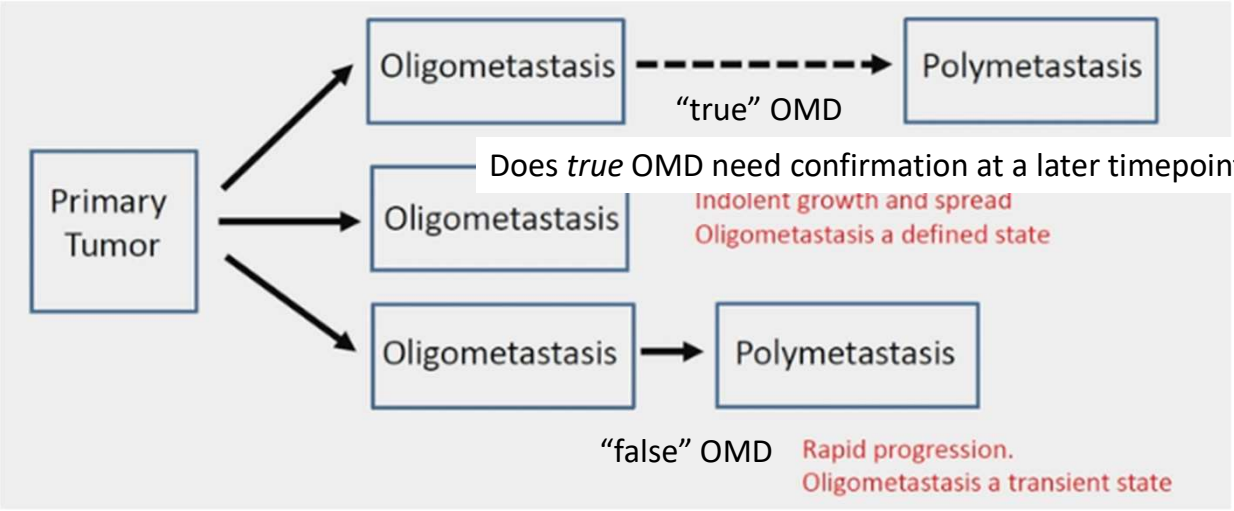

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Related Definitions and "Disease Burden"

- The oligometastatic state may be related to other measures of disease burden
- "Low-volume" (CHAARTED)
  - Exclusion: Either of the following: (a) ≥4 bone metastases on bone scan, with ≥1 outside the vertebral bodies or pelvis or (b) visceral metastases
  - OS benefits shown for abiraterone acetate, enzalutamide, apalutamide, and prostate-directed RT in *de novo* disease
- "Low-risk" (LATITUDE)
  - Exclusion: Any two of the following: (a) ≥3 bone metastases on bone scan, (b) Gleason score ≥8, or (c) Visceral metastases
  - OS benefits shown for abiraterone acetate in *de novo* disease
- Are "low volume" or "low risk" metastasis akin to oligometastatis?

Kyriakopolous et al. JCO 2018 36:1080-1087; Hoyle et al. Eur Urol (2019) *in press*

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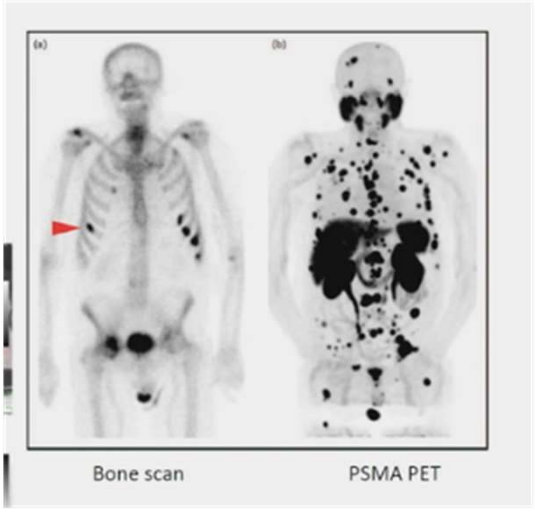

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Impact of Imaging on Defining Metastatic State

- Most published studies based on conventional imaging (MRI, CT, bone scan) and first generation molecular (NaF, choline, acetate)
- Definition and diagnosis of oligometastasis will depend on staging modality
- Significant reclassification (upstaging) clearly occurs with molecular imaging (PSMA, axumin)
  - non-metastatic to oligometastatic
  - oligometastatic to polymetastatic
  - Extrapolation of clinical data obtained with CI to that obtained with PSMA may NOT be warranted
- Also remember, even the best molecular imaging tool will miss (understage) a significant percentage of metastases (< 5mm, low PSMA)
  - In high risk patients, Ga-PSMA has a 30-40% sensitivity on per patient basis for nodes and a 24% sensitivity on a per node basis (Yaxly et. Al Journal of Urology 2019)

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- Tailor the definition to
  - "detectable" metastasis
  - the time interval between diagnosis of primary and diagnosis of oligometastasis
  - the nature of the primary tumor
- Generic definition
  - Metastatic with limited burden
  - 1-5 metastasis

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Metastasis-directed therapy

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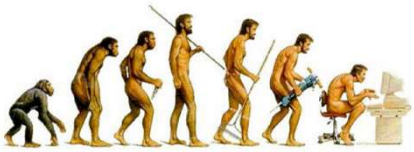

SBRT/SRS

- High precision
- High dose per fraction
- Small target volume
- Limited number of fractions (1-8)

- Non-invasive treatment
- High local control (70-100%)
- Few toxicities and low treatment mortality

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- The goal?
  - Treatment (de-)intensification
  - *True* OMD: curation?
  - Different settings
    - De novo
    - Oligorecurrence
    - Oligoprogression

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- Evidence?

- Future = bright, multiple phase 2 trials
- Final demonstration of benefit of focal therapies of oligometastasis *ideally requires unbiased phase 3 trials*
- Plenty of ongoing trials

Recurrent setting: STOMP (ADT-FS), ORIOLE (DFS), RADIOSA (cPFS)
De novo+ recurrent setting: EXTEND (PFS)
WOLVERINE meta-analysis (incl SABR-COMET, CRPC-FS, OS)
mCRPC: ARTO (BCR), MEDCARE (NSTFS)

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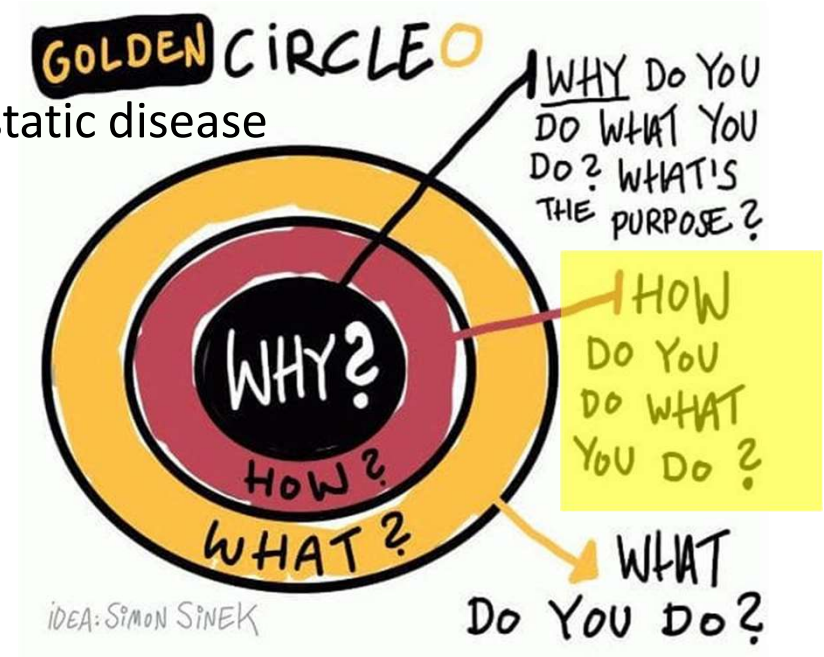

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How?

- Patient selection
- Simulation
- Prescription
- Treatment planning
- Delivery

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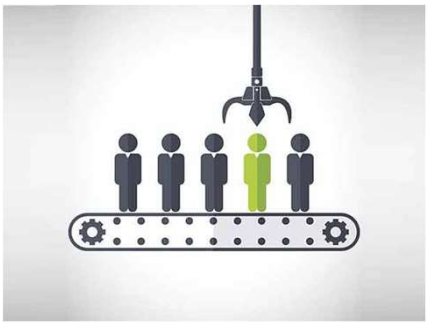
How?

- Patient selection
  - Multidisciplinary board meeting
  - Based on the latest evidence



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- Simulation
  - Immobilization
  - 4DCT (locations susceptible to respiratory motion)
  - Slice thickness of the CT: 1mm thickness
  - Use of contrast (e.g. in case of LN, cave bone)

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- Prescription

ICRU REPORT No. 91

PRESCRIBING, RECORDING, AND REPORTING OF STEREOTACTIC TREATMENTS WITH SMALL PHOTON BEAMS

- Need to specify what dose and to what % PTV

e.g. Prescribe 30 Gy to isodose covering 95% PTV

- Risk-adapted dose prescription (depending on location of the metastasis and surrounding organs at risk)

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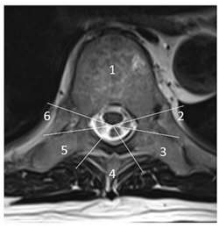
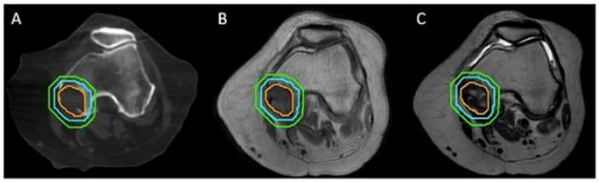
- Treatment planning
  - GTV: use all available imaging (fusion), usually 2+ modalities
  - (CTV): intraosseus (extraosseus when soft tissue disease a/o significant cortical bone disruption), not used for LN
  - (ITV): when 4DCT
  - PTV: margins depend on delivery system, approx 2-5 mm
  - OAR (spinal cord, plexus,…)





Clinical and Translational Radiation Oncology
Volume 45, March 2024, 100716

Practice and principles of stereotactic body radiation therapy for spine and non-spine bone metastases

Laura Burgess [a], Eric Nguyen [b], Chia-Lin Tseng [a], Matthias Guckenberger [c], Simon S. Lo [d], Beibei Zhang [a], Michelle Nielsen [a], Pejman Maralani [e], Quynh-Nhu Nguyen [f], Arjun Sahgal [a]

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- Treatment planning
  - IMRT/VMAT (FFF)
  - RESPECT accepted dose constraints from international datasets (AAPM TG101, UK consensus Diez,…)

Table 4
Pelvic constraints

Structure (standard nomenclature)	Metric	One fraction		Three fractions		Five fractions		End point (if available, from AAPM [18])
		Optimal	Mandatory	Optimal	Mandatory	Optimal	Mandatory	
Bladder	$D_{0.1cc}$		18.4 Gy [18,25]		28.2 Gy [18,25]		38 Gy [18,25]	Grade 3 cystitis/fistula
Bowel_Large	$D_{0.1cc}$		18.4 Gy [18,25]		28.2 Gy [18,25]		38 Gy [18,25]	Grade 3+ colitis/fistula
FemurHeadNeck	D_{10cc}	14 Gy [18,25]		21.9 Gy [18,25]		30 Gy [18,25]		Grade 3+ necrosis
LumbSacPlex	$D_{0.1cc}$	16 Gy [18,25]		24 Gy [18,25]		32 Gy [18,25]		Grade 3+ neuritis
	D_{5cc}	14.4 Gy [18,25]		22.5 Gy [18,25]		30 Gy [18,25]		
Rectum	$D_{0.1cc}$		18.4 Gy [18,25]		28.2 Gy [18,25]		38 Gy [18,25]	Grade 3+ proctitis/fistula
Ureter	$D_{0.1cc}$		35 Gy [25]		40 Gy [25,43]			
Urethra	$D_{0.1cc}$		Report		Report		Report	

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- Delivery
  - High resolution MLC linac/cyberknife/tomotherapy
  - IGRT: daily 3D kilovoltage CBCT imaging
  - 6 degrees of freedom couch
  - Intrafraction motion technology (tumor tracking ExacTrac, gating,..)
  - Consider intrafraction CBCT when treatment delivery length > 20min or when suspected patient movement
  - Optional post-treatment CBCT to document stability of the target during treatment
  - *Emerging technologies: MR-LINAC, proton therapy (FLASH),…*

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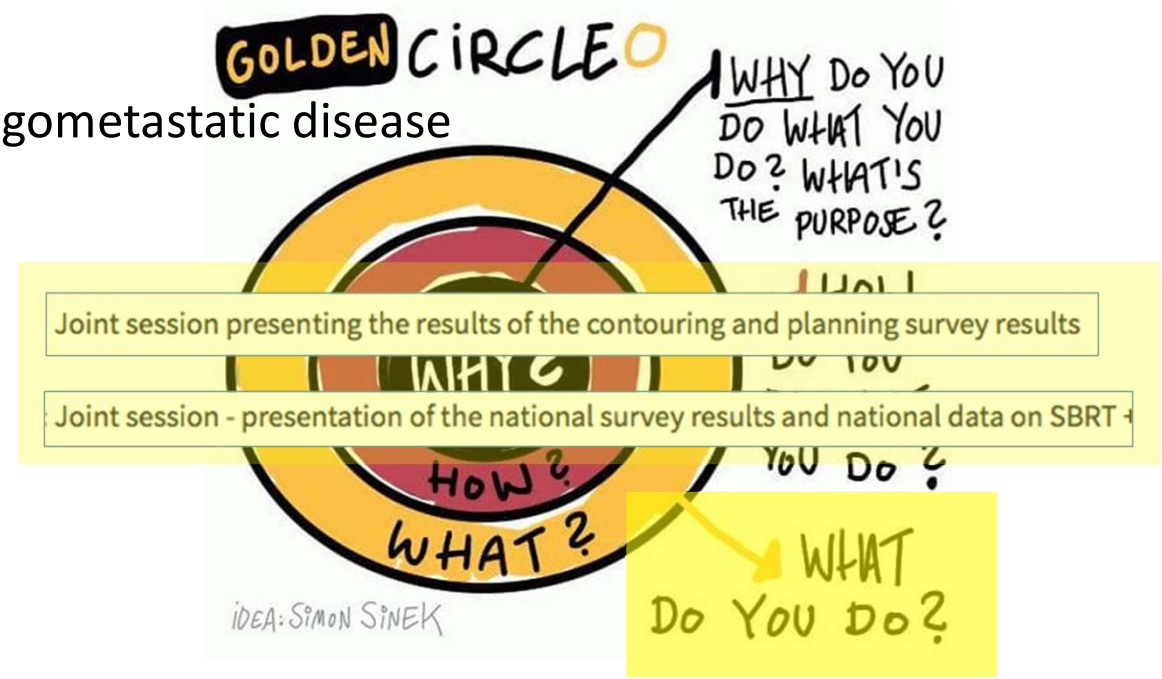

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