The sense and non-sense of radiotherapy and radiofrequency ablation to control isolated lung metastases

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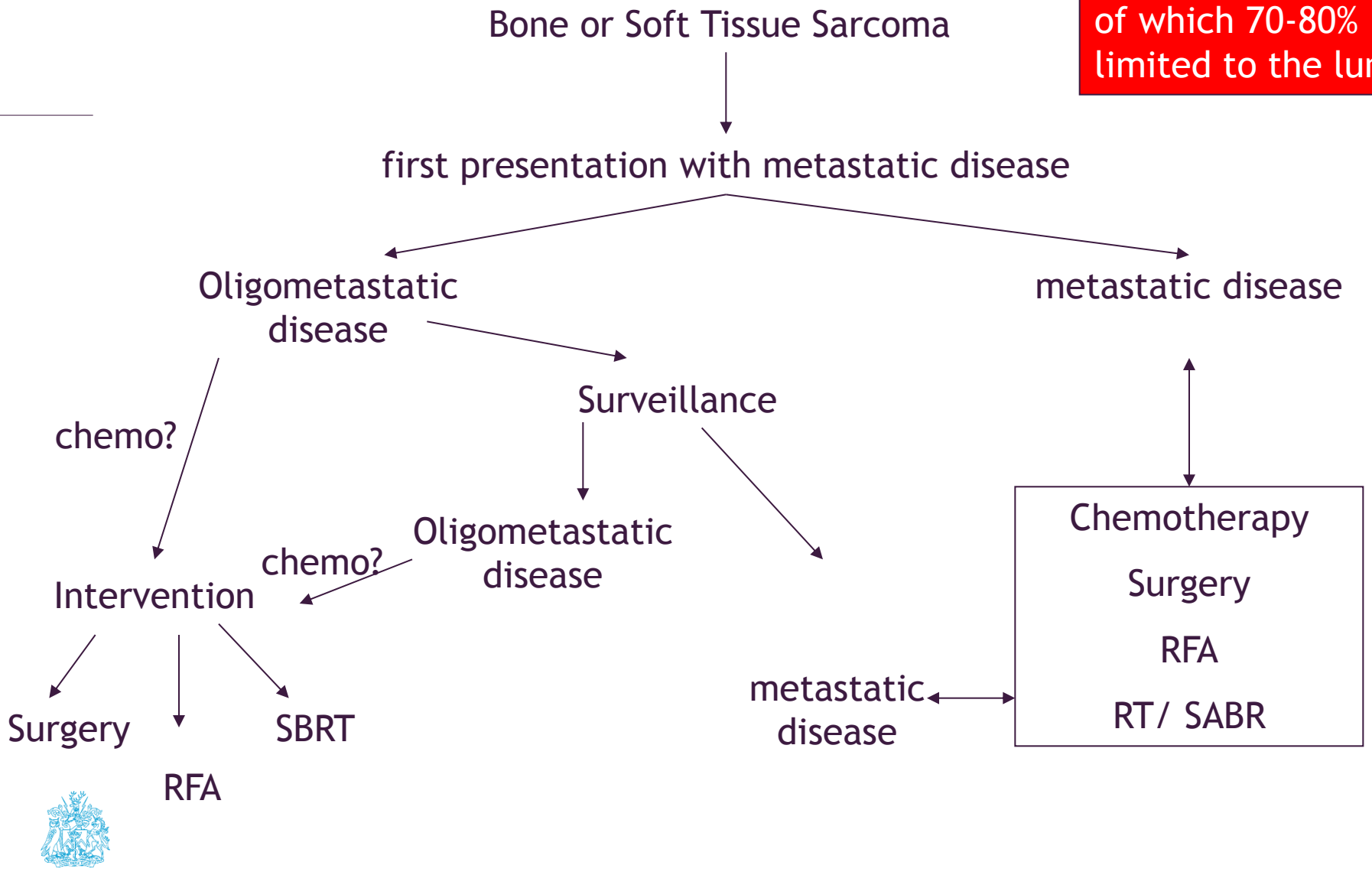
40-60% develop metastatic disease of which 70-80% limited to the lungs



Define oligometastatic disease

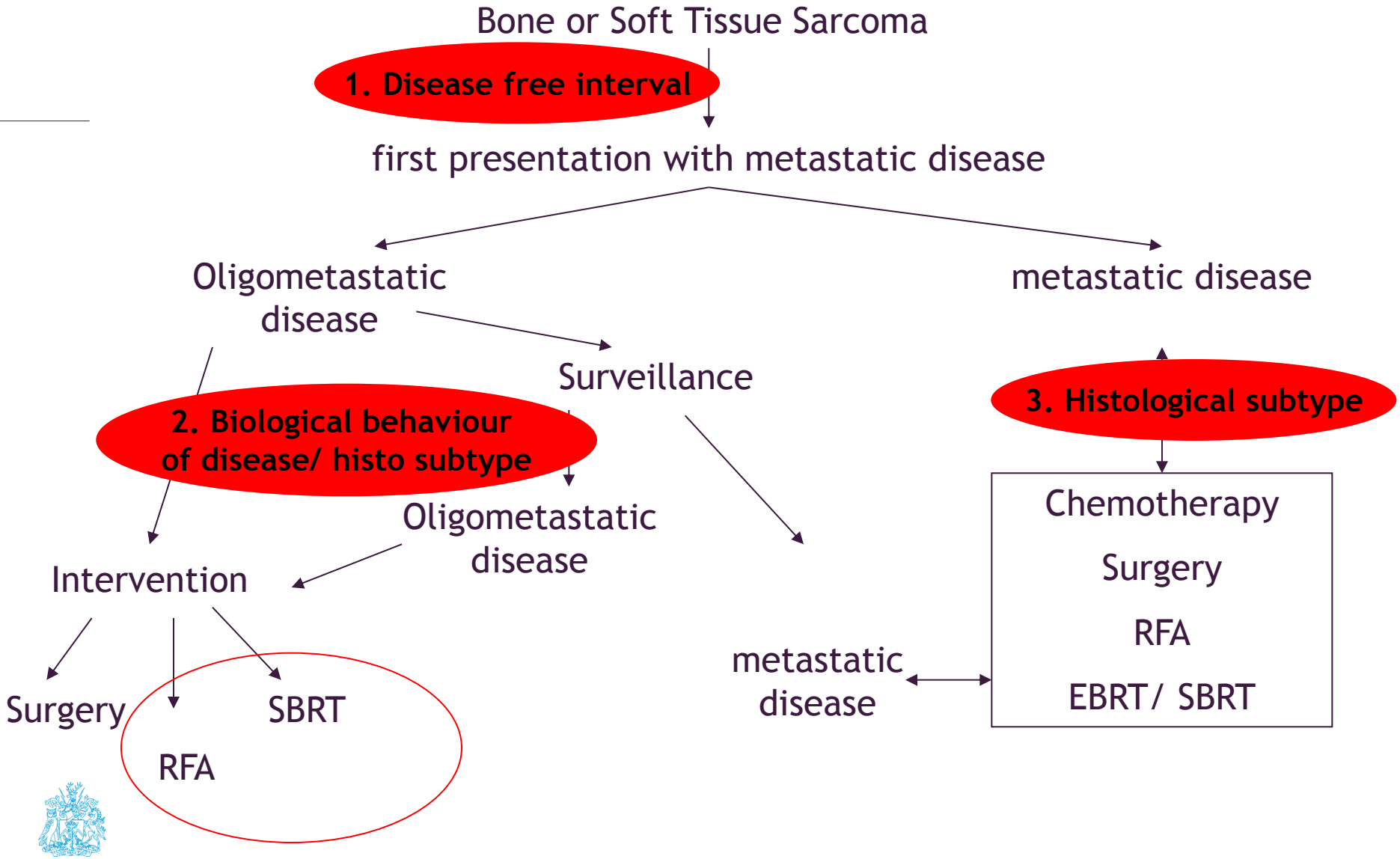
1. Oligometastatic disease is an intermediate state of cancer spread between localised disease and widespread metastatic disease

2. The metastases are limited to a single or limited number of organs or number of lesions <5

3. Patients with oligometastatic disease may be amenable to a curative therapeutic strategy

Hellman and Weischselbaum, 1995

Selecting patients for a 'curative' strategy

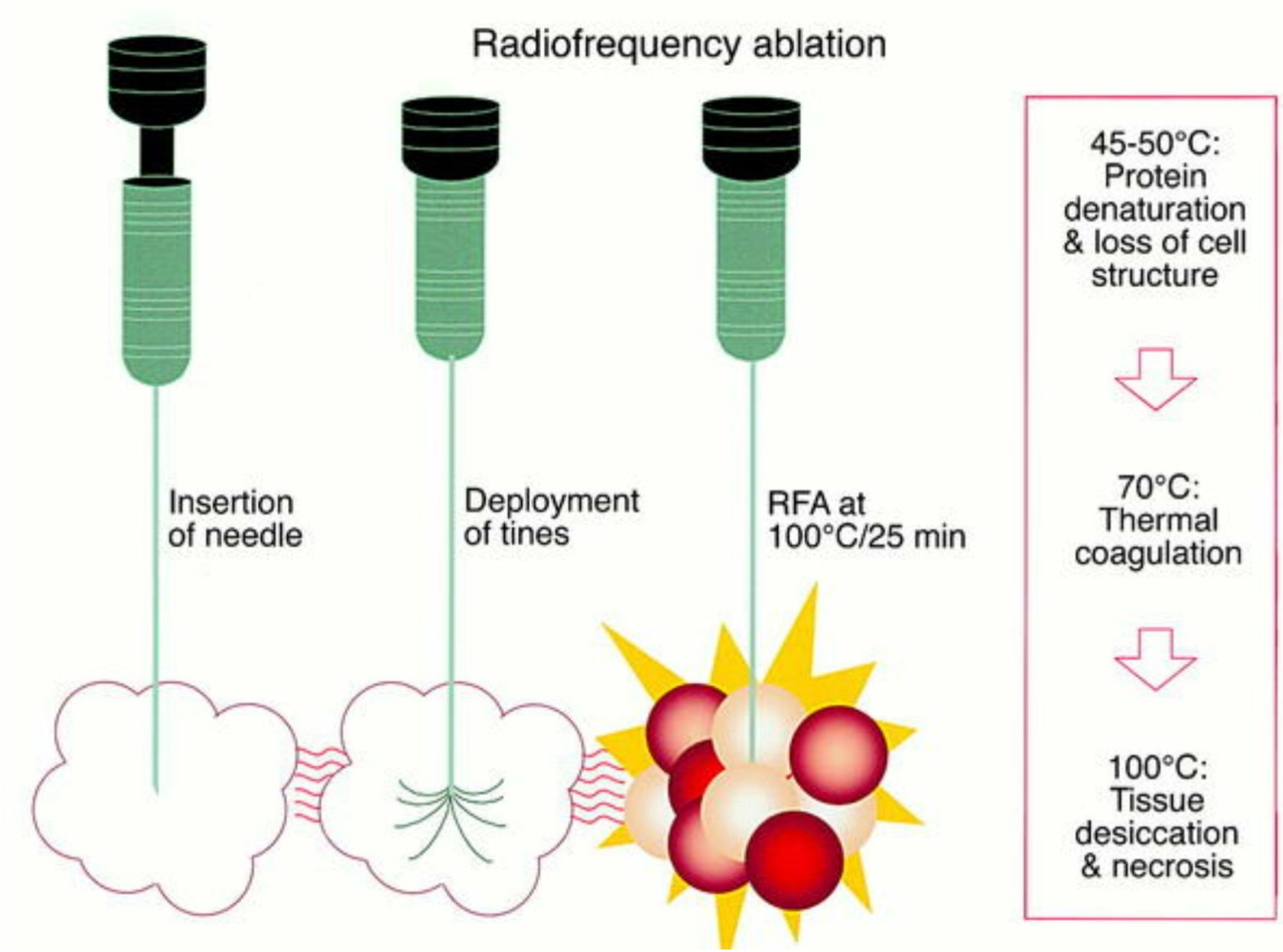


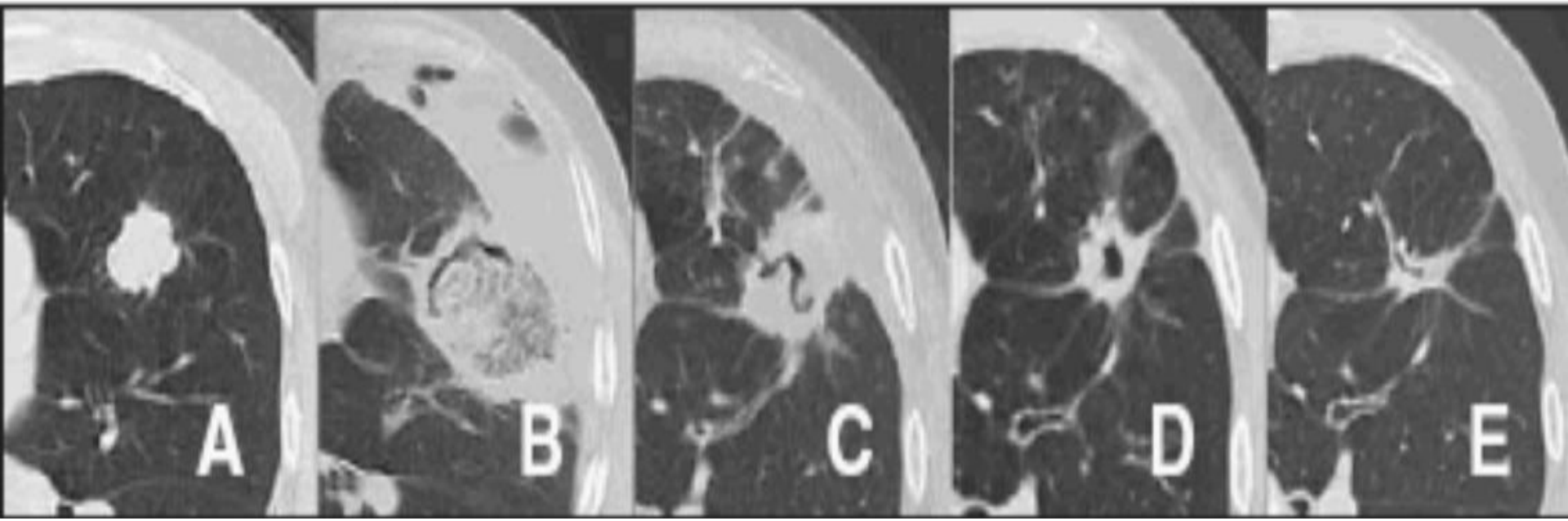
Procedure

1. Sedation/anaesthesia
2. CT fluoroscopy
3. ~12-25 minutes
4. Chest drain if pneumothorax>3cm

Indications for radiofrequency ablation (RFA)

1. Maximum number of lesions for one RFA session~3
2. Maximum size of lesion~4-5cm
3. Location:
   i. avoid lesions <1cm from hilum, large vessel, main bronchus, oesophagus or trachea or
   ii. direct contact with vessels ≥3mm diameter or myocardium
4. Path of needle tract must avoid
   Large vessels
   Bronchi
   Blebs
   Fissures


Radiofrequency ablation
Insertion of needle
Deployment of tines
RFA at 100°C/25 min
45-50°C: Protein denaturation & loss of cell structure
70°C: Thermal coagulation
100°C: Tissue desiccation & necrosis



A: pre-ablation

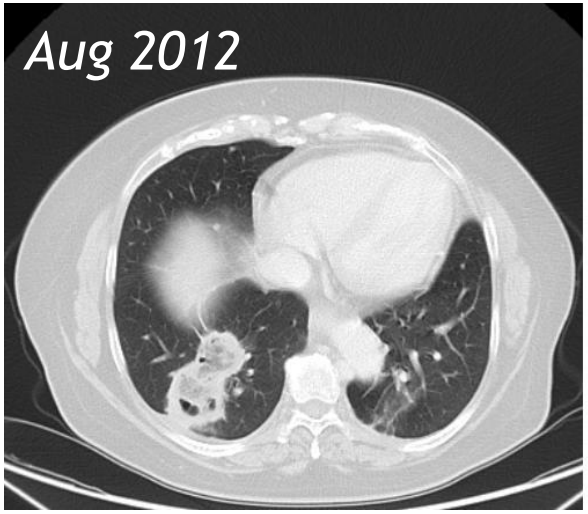
B: 1 month post ablation

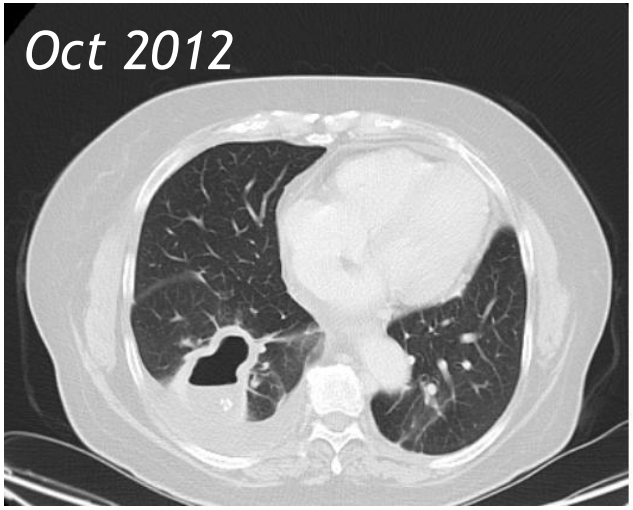
C: 3 months post ablation

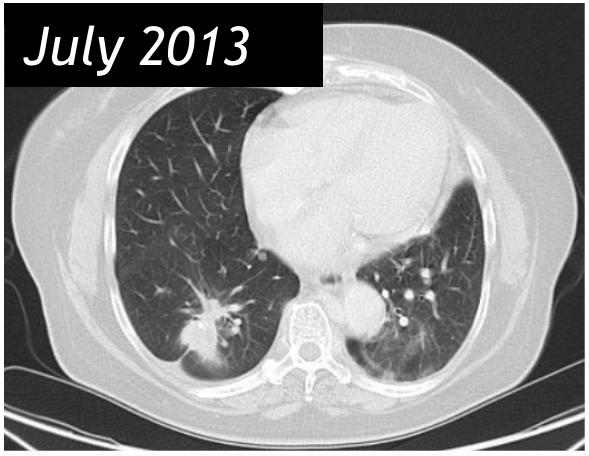
D: 6 months ablation

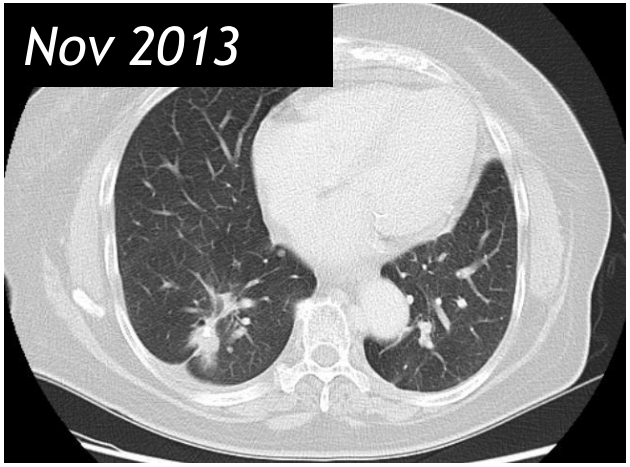
E: 12 months post ablation

RFA and pazopanib: 61 yr old lady, RFA July 2012, started pazopanib 2 weeks later. Oct 2012, developed chest pain and haemoptysis, stopped pazopanib, recommenced Jan 2013





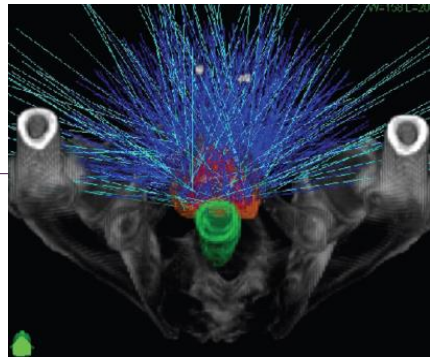


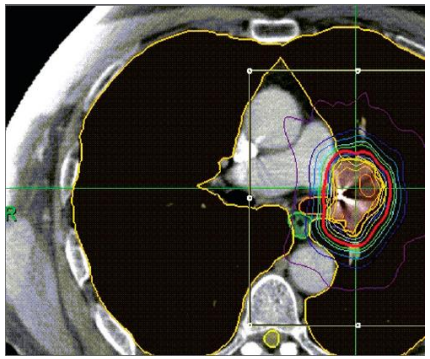


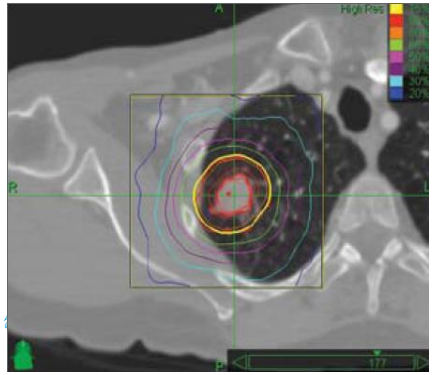
Other forms of thermal ablation

1. cryoablation
2. microwave ablation
3. laser interstitial tumour therapy

stereotactic ablative body radiotherapy (SABR)/SBRT







Highly conformal RT, delivering RT via 100 fine pencil beams to treat a lesion measures <6cm diameter

Treatment takes 1 hour

Much more focussed on the tumour hence less dose to normal tissues
Tracks the tumour during treatment hence less chance of a 'miss'

Large ablative doses: 40-50 Gy

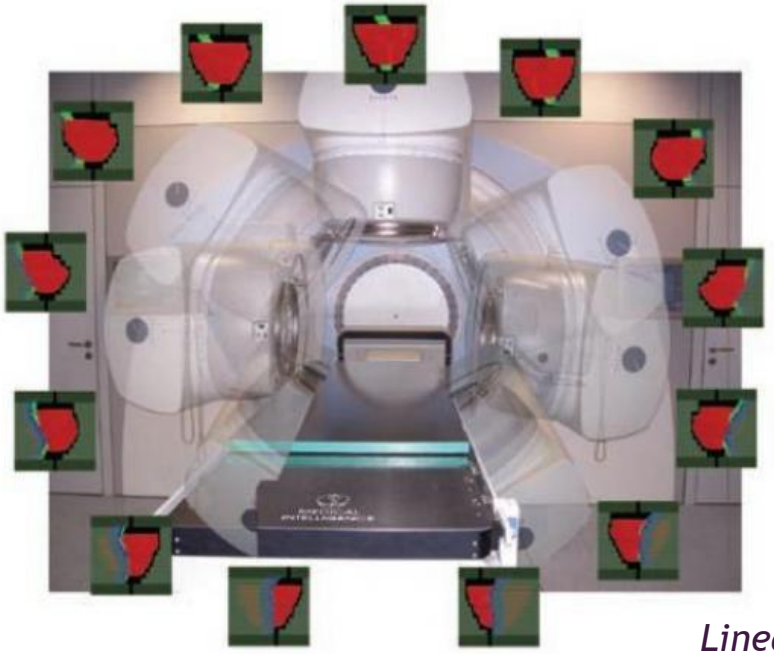
1. 3#
2. 5#
3. 10# (especially if lesion within 2cm of the central no fly zone)

EQD2 (equivalent dose at 2 Gy/#: can be from 60Gy to 140-200 Gy)

Indications for stereotactic ablative body radiotherapy (SABR)/SBRT

1. Lesions <6cm in size
2. Commonly when lesions are not amenable to metastasectomy or RFA
3. Lesion amenable to tracking , eg fiducial markers or respiratory gating

Cyberknife

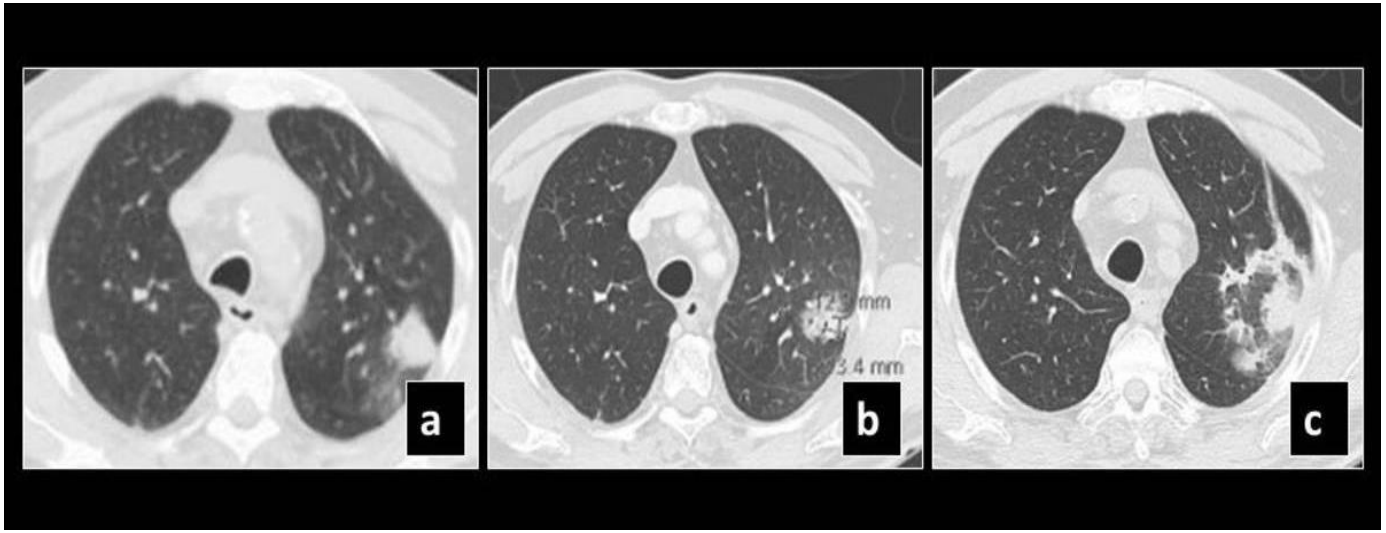


Linear Accelerator

Checklist

1. Lung function tests
2. Insertion of fiducial markers
3. Planning CT scan
4. Funding!

Response assessment after SBRT



Pre SBRT CT (a) shows a left upper lobe lesion, which 5 months post SBRT became more ground glass opacified (b) and 9 months later (c) it demonstrated the orbit sign' characterized by the presence of a central lesion surrounded by an inner zone of relatively spared lung and an outer zone of ground-glass opacifcation or consolidation .

Khanda ESR, 2014

- But do these local therapies offer improved outcomes….
  - Progression free survival
  - Overall survival
  - Where’s the evidence?

radiofrequency ablation

Reference	Number of patients	Number of metastases	Median follow up	PFS	OS	Complications
Nakamura 2009	20 (80% received chemotherapy) (55% previous surgery)	89	2002-2007 18 months	NR but 54% developed further lung metastases	3 yr: 29% Complete ablation significant prognostic factor	Pneumothorax: 65% Chest drain: 38%
Pennathur 2009	22 (23% previous surgery) (18% sarcoma)	27	2001-2005 29 months	NR	Est 2 yr: 68%	Pneumothorax: 70%
Palussiere 2011	29	47	2002-2009 50 months	DFS : 7 months (3.5-10)	3yr: 65%	Pnuemothorax: 69%
Von Meyenfeldt 2011	46 26% sarcoma (78% previous surgery)	90	2004-2009 22 months	2 yr: ~22%	3yr:~ 69%	Pneumothorax 34% Chest drain 25%
Koelbinger 2014	22	55	2007-2012 20 months	2 yr: 23%	3yr: 85% Disease free interval impacted on OS	Grade 3 toxicity: 7%

stereotactic ablative body radiotherapy

Reference	Number of patients	Number of metastases	Median follow up	PFS	OS	Dose delivered
Stragliotto 2012	46	136 (97 lung)	1994-2005 22 months	Nr 2 yr local control 90%	3 yr: 34%	20 Gy/1# 24 -45 Gy/3# 24-48 Gy/4# 20-40 Gy/5#
Dhakal 2012	52 15 SBRT	74	1990-2006 12 months	3yr local control : 82%	Median OS: 2yrs	50 Gy/5#
Mehta 2013	16 All received chemo 38% prior metastectomy	25	2009-2011 20 months	nr	4yr: 72%	54 Gy/3# 50 Gy/4# 36 Gy/3# 42 Gy/3#
Singh 2014	34 (4 sarcoma)	49	2008-2011 17 months	nr 3yr local control : 82%	2yr: 44%	40 Gy/5# 45 Gy/5# 50 Gy/5# 60 Gy/5#
Soyfer 2014	22	53	95 months	nr	5yr: 62%	
Merrell 2014	21 (50% lung)	30	2008-2013 24 months	nr	2yr: 58% 4yr: 12.5%	50Gy/5#

Current studies:

NCT01949506: SBRT and ART for pulmonary metastases from soft tissue sarcoma, N=20, 1-5 mets, <5cm

Primary endpoint: acute toxicities from SBRT

Secondary endpoints: local control, disease free survival, overall survival, quality of life

Estimated 5 year overall survival for STS:

- All cases: 15%[1]
- Pulmonary metastasectomy: 25%[2]
- RFA: 30%[3]
- SABR: ~20%[4]

1. *Thames cancer registry 1995-2004*
2. *Treasure BMJ 2012*
3. *Nakamura Cancer 2009*
4. *Dhakal IJROBP 2012*

In conclusion

There is sense in considering a non-surgical approach

1. Avoid an operation
2. Low morbidity
3. Minimal collateral lung damage

However…

- there is a selection bias which may make it impossible to determine which is superior?

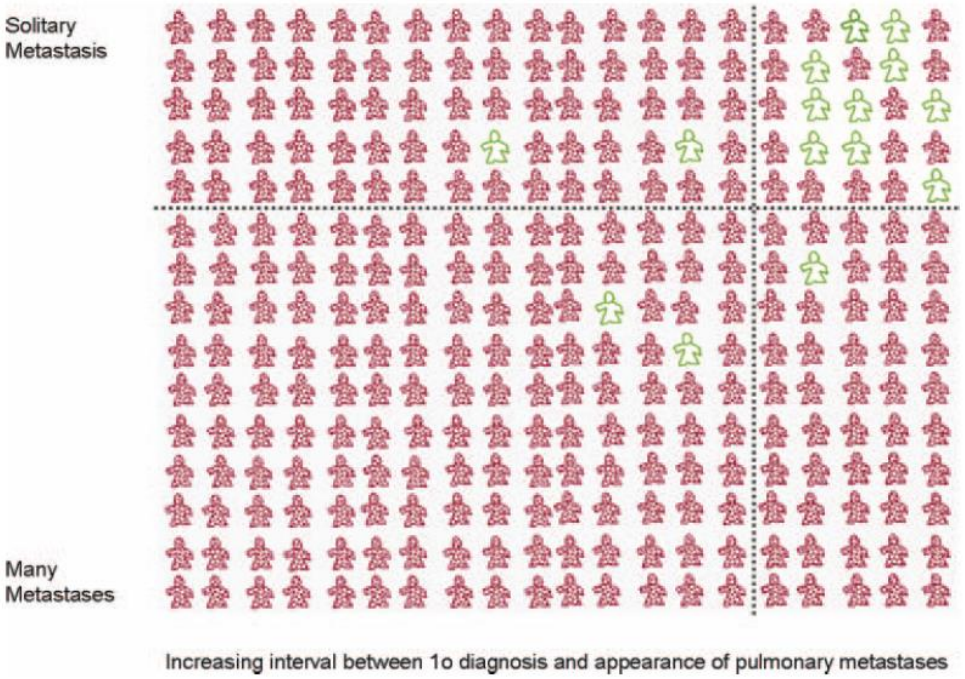
So …currently, best practice

1. individualise according to
   - disease free interval
   - histological subtype
   - true oligometastatic disease

CASE SELECTION

2. Discussion in the context a thoracic sarcoma MDT
   - Prospectively collected database of survival outcomes and complications to establish criteria for use of the different treatment modalities

3. Need to establish the evidence to determine impact on PFS and OS



Treasure 2012

What we really want to know is whether we have a robust decision-making process that delivers consistency, and of course whether our approach is clinically worthwhile at all……