

Preoperative Embolization in Surgical Treatment of Spinal Metastases:

Single-blind, randomized controlled clinical trial of efficacy in decreasing intraoperative blood loss

Lars Lonn on behalf of my co-authors
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- No relevant financial relationships disclosed



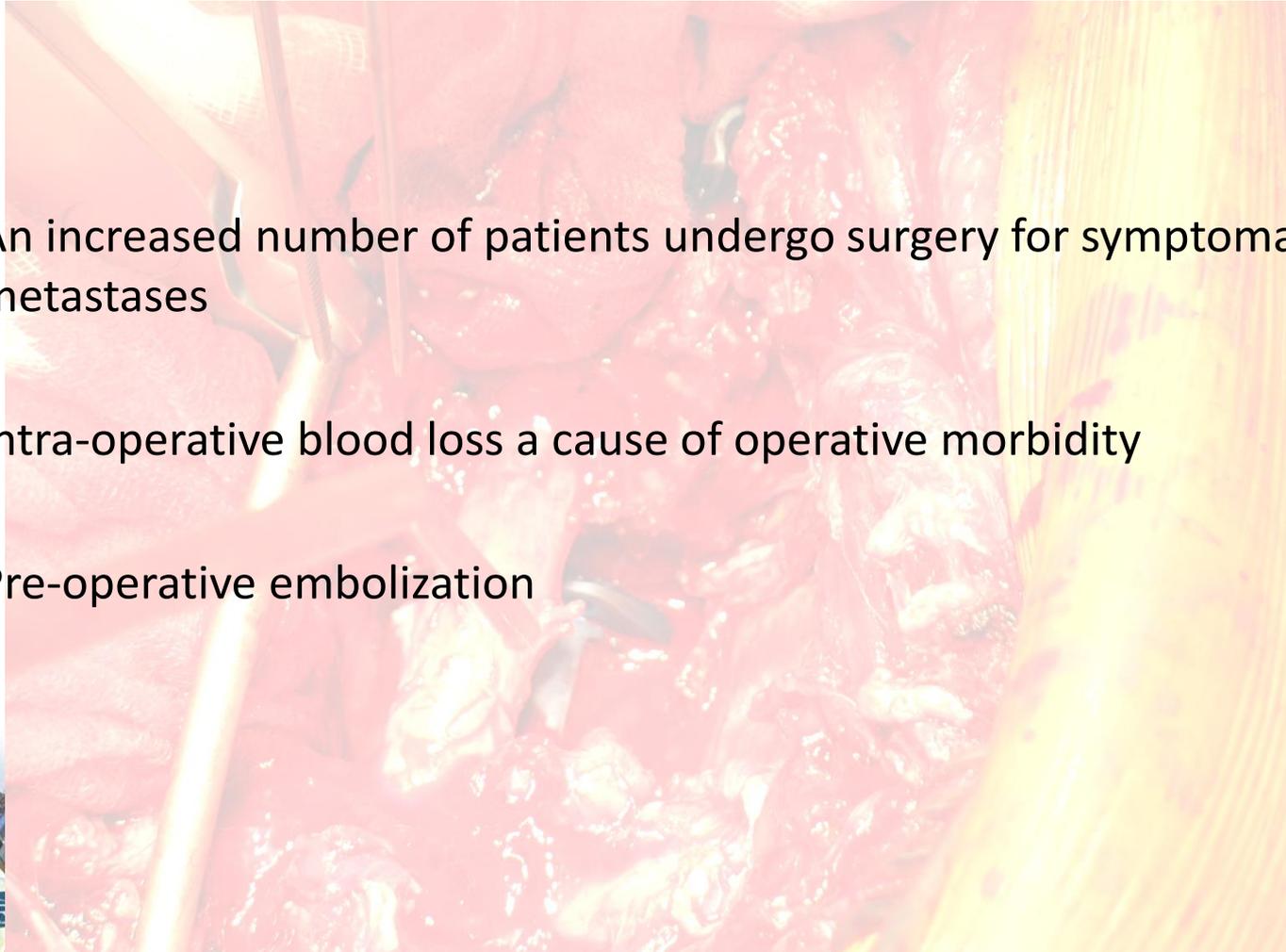
Background

- In Denmark 30 000 per year are diagnosed with cancer (www.ssi.dk)
- Life expectancy with advanced cancer has increased (www.sundhedsstyrelsen.dk)
- A common complication of advanced cancer is bone tissue metastases
 - especially to the spine
- 5-14% experience symptomatic compression of the spinal cord or cauda equina (Patchell 2005, Klimo 2004)
- Symptoms (Cole 2008):
 - pain
 - impaired motor, sensory and autonomic functions
 - mechanical instability of the spine



Background

- An increased number of patients undergo surgery for symptomatic spinal metastases
- Intra-operative blood loss a cause of operative morbidity
- Pre-operative embolization



Treatment options

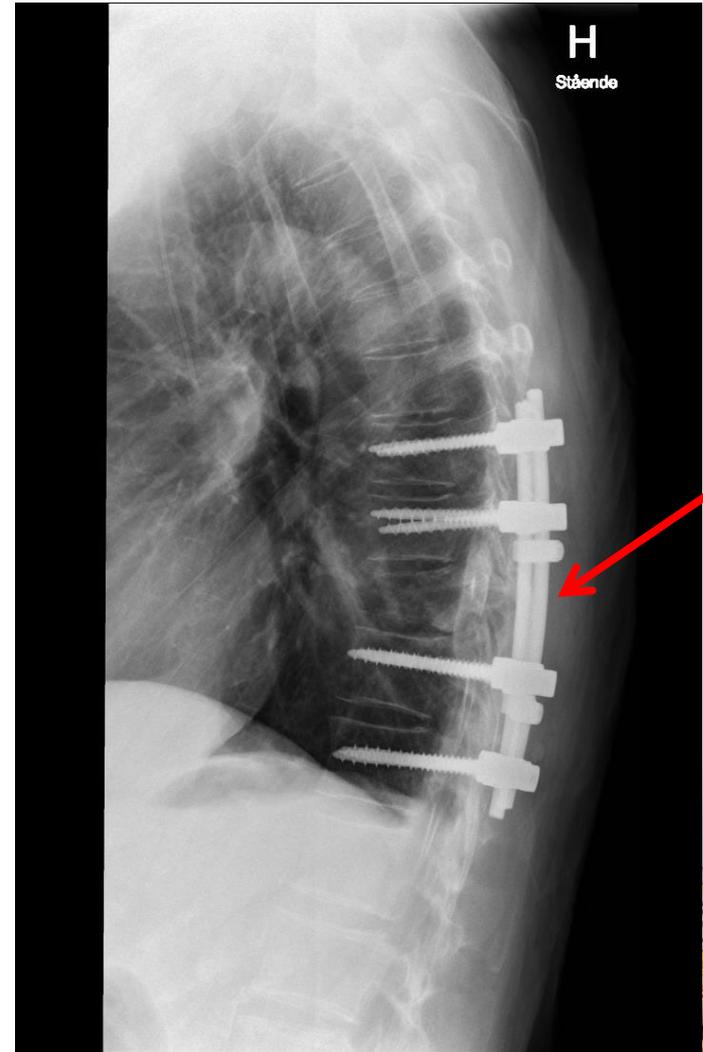
Individually planned according to stage of disease, surgical risk and prognosis:

- Corticosteroids, analgesics and sometimes chemotherapy
- Combined with:
 - open surgery followed by radiotherapy
 - radiotherapy alone



Open surgery followed by radiotherapy

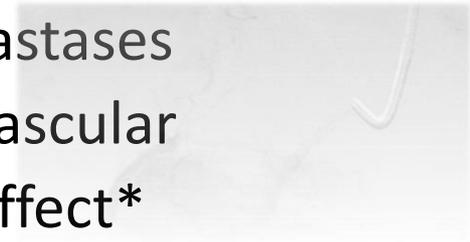
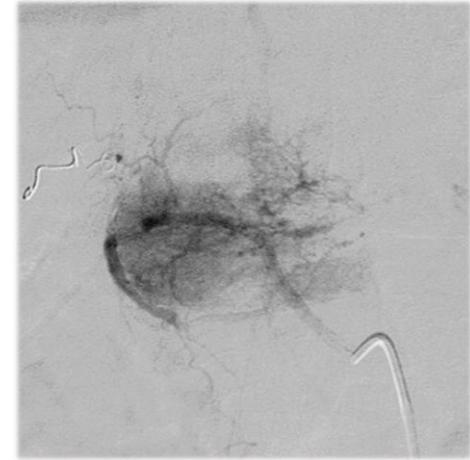
- Increasing evidence:
Surgical decompression and instrumented stabilization followed by radiotherapy results - better outcome than radiotherapy alone (Patchell 2005, Kim 2012, Ibrahim 2007, Quan 2011, Klimo 2005)
- Associated with significant blood loss and a risk of catastrophic blood loss (Chen 2013 – Meta-analysis)
 - 18 papers, 760 patients
 - Mean 1828 mL
 - 12 % >5500 mL



Background

Previous studies:

- Retrospective
- Long study periods
- Conflicting conclusions
- Renal and thyroid cancer
- Hypervascularity is found in metastases
not generally considered hypervascular
- Approximately 50:50; effect:no effect*



*Berkefeld et al, Am J Neuroradiol 1999; Kobayashi et al, Acta Radiol 2012; Prabhu et al, J Neurosurg 2003; Thiex et al, Spine J 2013; Wirbel et al, J Orthop Sci 2005; Robial et al, Orthop Traumatol Surg Res 2012; Wilson et al, Am J Neuroradiol 2010; Nair et al, Interv Neuroradiol 2013; Schmidt et al, Tumori 2011; Hess et al, Arch Orthop Trauma Surg 1997; Gellad et al, Radiology 1990.

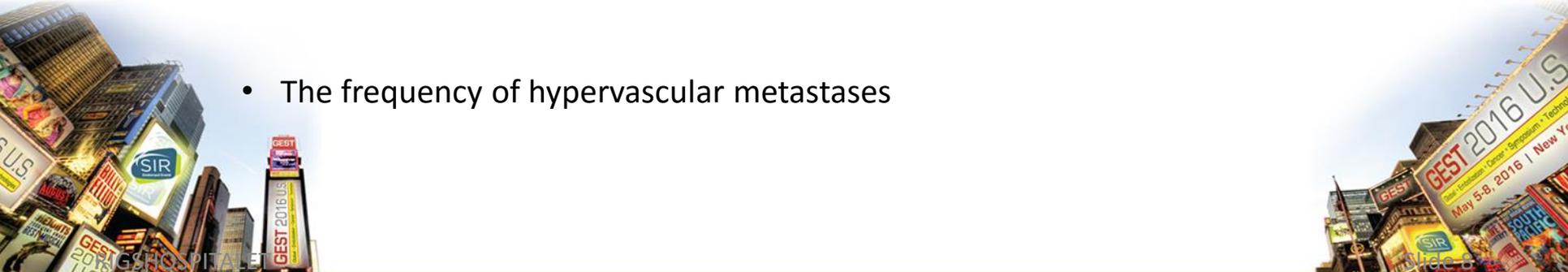


Aim of Study

To assess whether pre-operative embolization of spinal metastases regardless of primary cancer reduces:

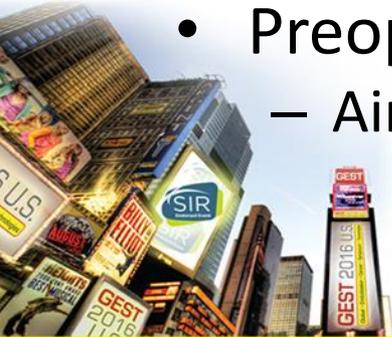
1. Intra-operative blood loss
2. Blood transfusions
3. Surgery time

- The frequency of hypervascular metastases



Reduction of intraoperative blood loss

- Antifibrinolytic agents (Elwatidy 2008)
- Controlled perioperative hypotension (Dutton 2004)
- Intraoperative cell salvage combined with a leucocyte depletion filter (Yuan 2013)
- Development of less invasive percutaneous techniques
- Preoperative arteriography and embolization
 - Aiming to reduce the vascularity prior surgery



Inclusion criteria

- ≥ 18 years
- Symptomatic metastatic compression of the spinal cord or cauda equina
- No contraindication to surgery
- Decompression and posterior thoracic and/or lumbar spinal instrumentation



Design

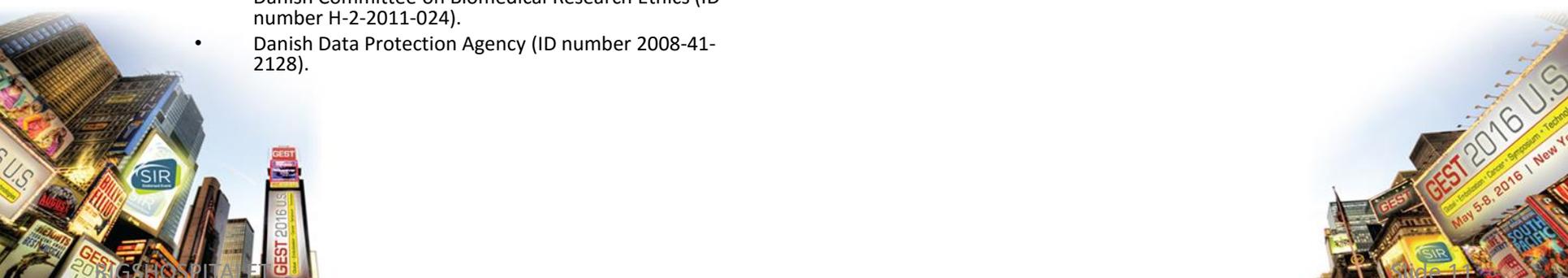
- Randomized controlled trial
- The CONSORT Statement

- Blinded:
 - Surgeons
 - Anesthesiologists assessing outcomes

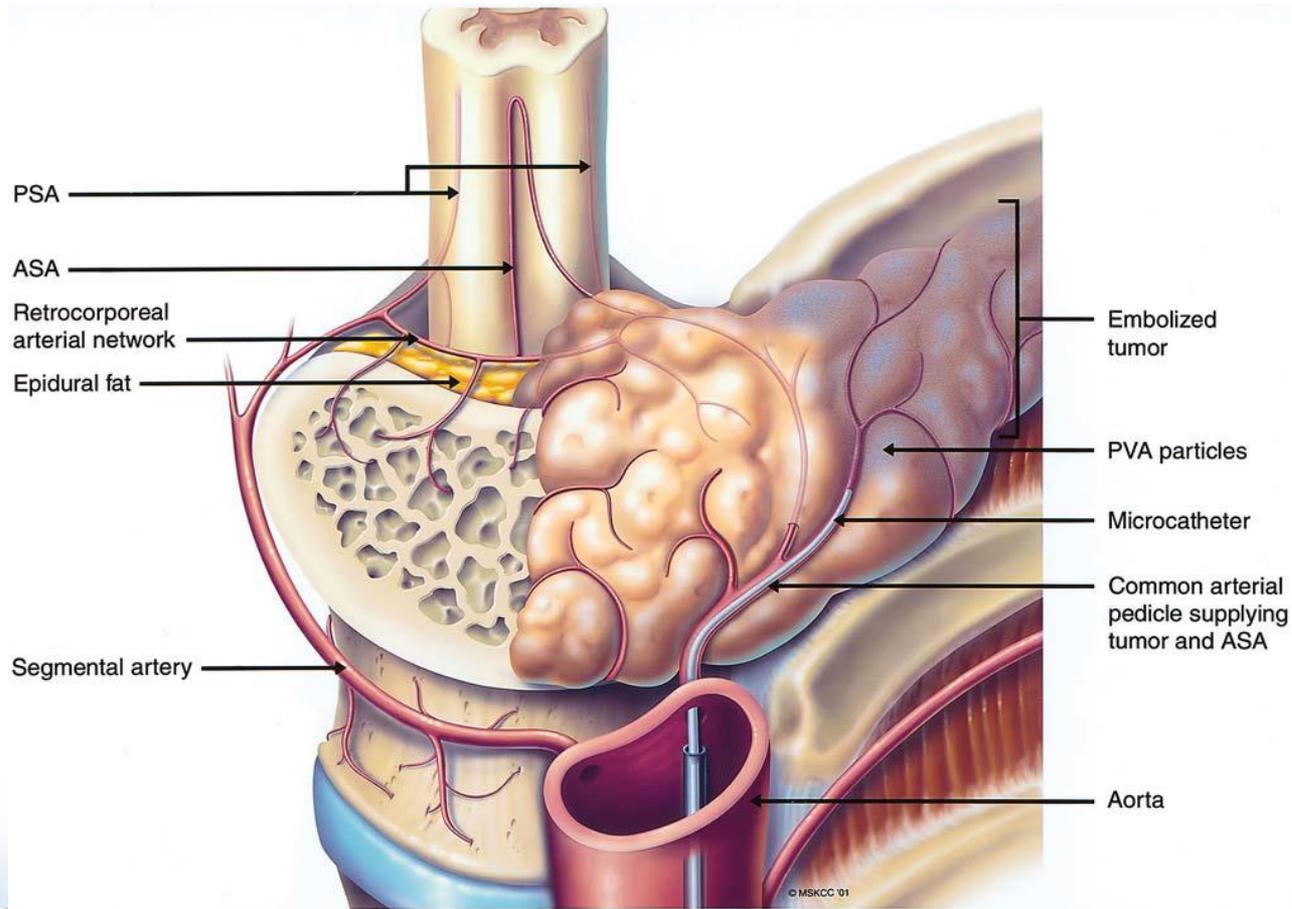
- Pre-registered at www.ClinicalTrials.gov (NCT01365715).
- Danish Committee on Biomedical Research Ethics (ID number H-2-2011-024).
- Danish Data Protection Agency (ID number 2008-41-2128).

Embolization group
- Angiography and embolization

Control group
- Angiography



Angiography and embolization



© Prabhu VC, Bilsky MH, Jambhekar K, et al. Results of preoperative embolization for metastatic spinal neoplasms. *J Neurosurg* 2003; 98:156-164.

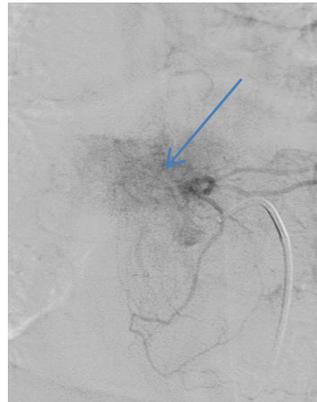


Angiography and embolization

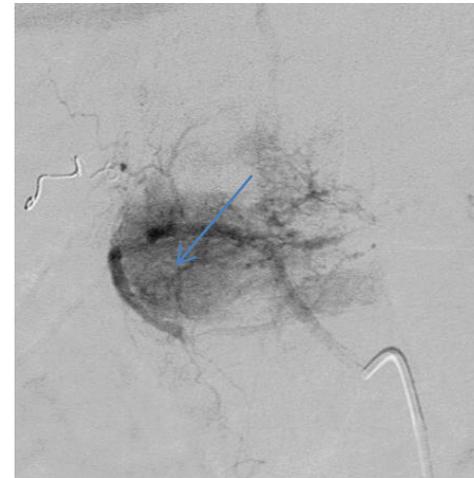
- Affected vertebra and two levels above and below
- PVA



No hypervascularity



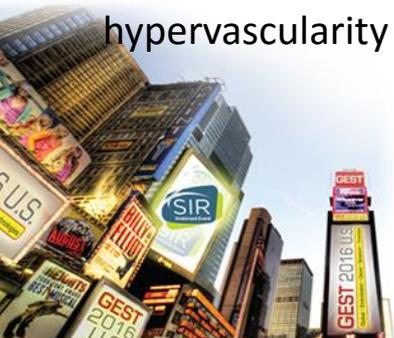
Moderate hypervascularity



Pronounced hypervascularity



Post embolization

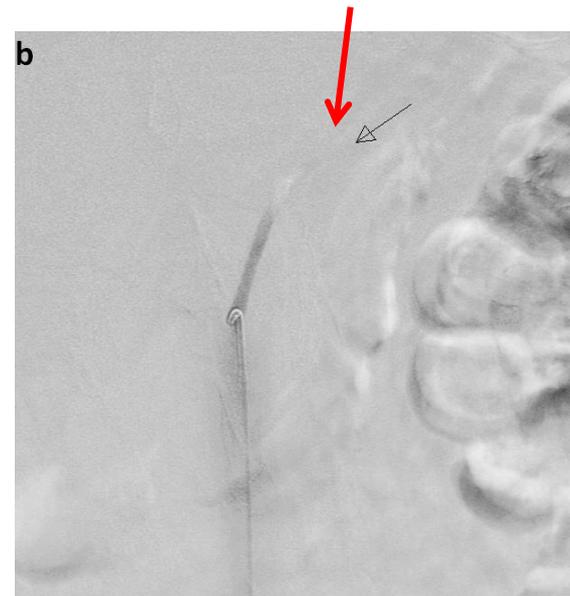


Embolization

- **300 μm PVA foam particles - preferred choice**
- 500 μm PVA foam particles - larger caliber vessels
- Gelatin sponge, micro coils
- Endpoint : complete exclusion of all arterial feeders



Pre-embolisation tumor blush



Pre-embolisation tumor blush



Angiography and embolization

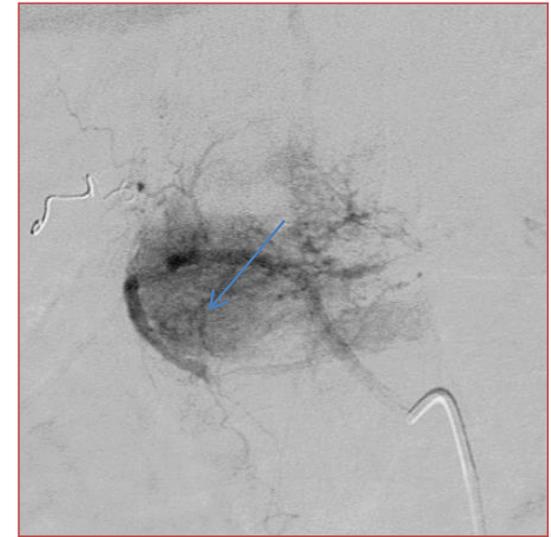
- 0-48 hours before the scheduled surgery
- Vascularity: Tumor blush intensity



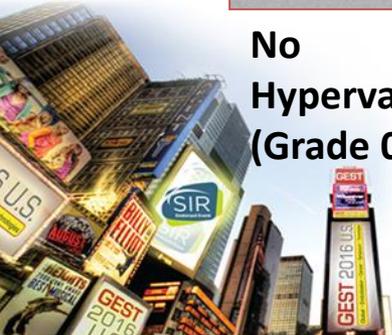
**No
Hypervascularity
(Grade 0)**



**Moderate
Hypervascularity
(Grade 1)**



**Pronounced
Hypervascularity
(Grade 2)**

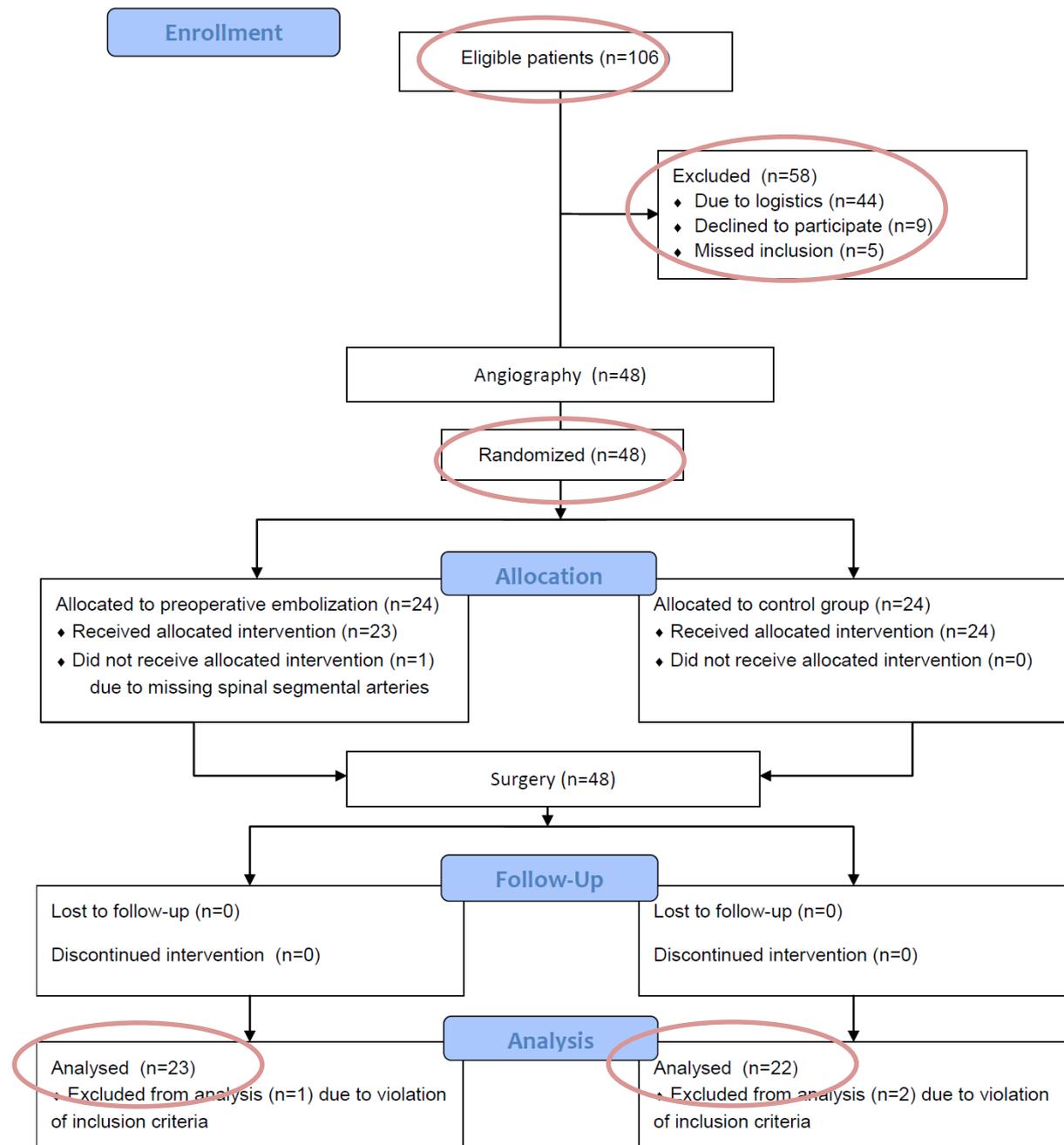


Statistical analyses

- **By intention-to-treat**
- The Independent t-test for comparison of continuous outcomes
 - when the assumptions of normality and homogeneity of variance were met
- The Mann-Whitney test when not
- Categorical outcomes: Chi-square test
- Fisher's exact test
 - if numbers of expected values were less than five
- P value < .05 (two-tailed) statistically significant
- Effect sizes were stated with 95% confidence intervals (CI)

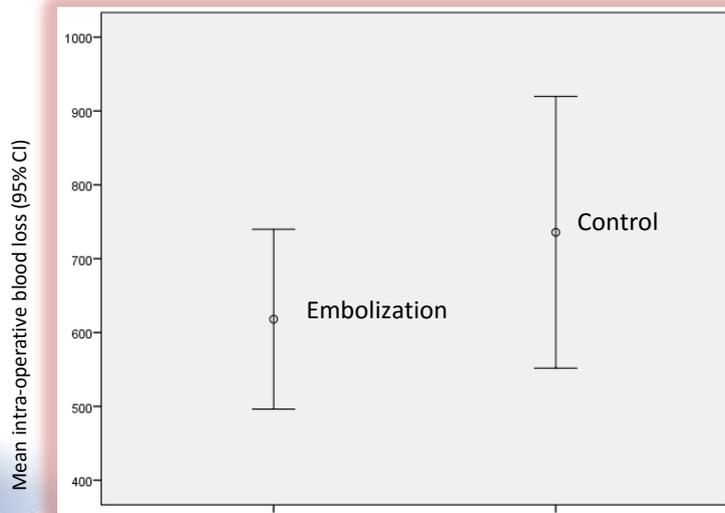


Enrollment:
May 2011-March 2013



Results

Embolization did not significantly reduce intra-operative blood loss:



- 620 mL (SD, 282 mL) vs. 740 mL (SD, 415 mL)
- Mean difference -120 (95% CI: -330 – 95)
- $P = .270$



Results

- No. of patients who received blood transfusions not significantly reduced in embolization group:
 - 2 (9%) vs. 5 (23%)
 - $P = .243$

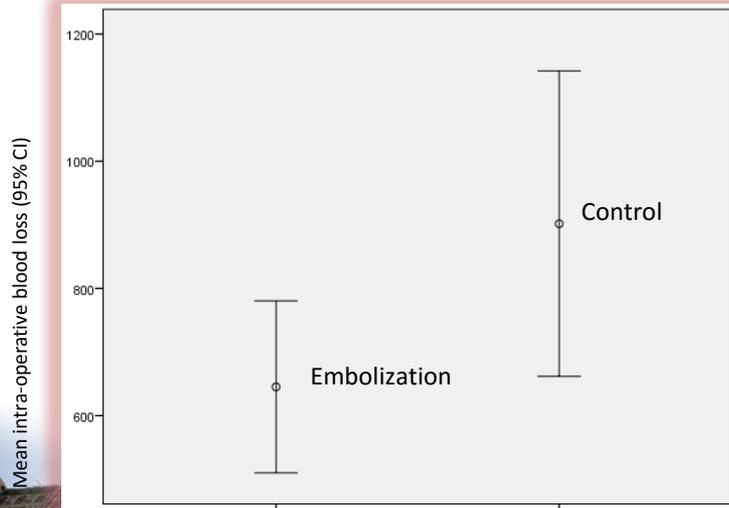
- 25% reduction of surgery time in embolization group:
 - Reduced 35 min
 - Median 90 min (range, 54-252) vs. 125 min (range, 80-183)
 - $P = .031$

– 34 of 45 metastases were hypervascular (76%)



Results

Blood loss significantly reduced in hypervascular metastases:



- 650 mL (SD, 289) vs. 900 (SD, 416).
- Mean difference -250 (95% CI: -502 - -11).
- $P = .041$



Conclusions

- Intra-operative blood loss and RBC transfusion not significantly reduced
- 25% reduction in surgery time
- Intra-operative blood loss significantly reduced in hypervascular metastases



Thank you

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PLOS ONE

On the Antiquity of Cancer: Evidence for Metastatic Carcinoma in a Young Man from Ancient Nubia (c. 1200BC)

Michaela Binder^{1*}, Charlotte Roberts¹, Neal Spencer², Daniel Antoine², Caroline Cartwright³

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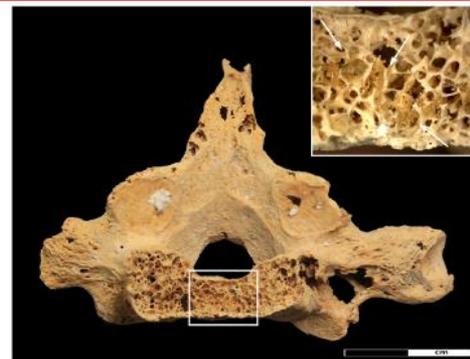


Figure 9. Destructive lesion in vertebral body of the 7th thoracic vertebrae. Detail of the pathological changes in the 7th thoracic vertebra. Rectangle indicates area of new bone infill of the spongiosa. Close-up of new bone formation indicated by arrows is shown in the insert; arrows indicate new bone formation.
doi:10.1371/journal.pone.0090924.g009

