

**PRESURGICAL TUMOR
EMBOLIZATION USING ONYX 18
RADIOGRAPHIC AND HISTOLOGIC EVALUATIONS**

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HISTORICAL PRETEXT

- 1904
 - Dawbarn injected liquid paraffin into the ECA to embolize malignant head and neck tumors
- 1970s
 - Serbinenko used detachable balloons for embolization of tumor supply

EMBOLIC AGENTS

- Three classes of embolic agents
 - Liquid agents
 - Onyx
 - NBCA (super glue)
 - ETOH
 - Hydrogels
 - Particulate agents
 - Embospheres (sized spherical particles)
 - Polyvinylalcohol (PVA; sized irregular shaped particles)
 - Gelfoam
 - Platinum coils
 - Fibered and Unfibered
 - Detachable and Nondetachable)

INDICATIONS

- Many studies have confirmed that preoperative embolization of CNS tumors is associated with:
 - Shorter operative time
 - Reduced blood loss
 - Decreased transfusion requirements
 - Reduced LOS
- Embolization of hypervascular tumors is therefore indicated to:
 - Control surgically “inaccessible” arterial feeders
 - Decrease surgical morbidity by reducing blood loss
 - Shorten operative procedure time
 - Increase the chances of complete surgical resection
 - Decrease the risk of damage to adjacent normal tissue
 - Relieve intractable pain
 - Decrease expected tumor recurrence
 - Allow better visualization of the surgical field

PROCEDURAL RISKS

- Stroke
- Death
- Tumor swelling with mass effect
- Headache
- Skin and muscle necrosis
- Facial pain
- Failure to achieve stated goal

ONYX

- Onyx (Covidien, Irvine, CA, USA)
 - Cohesive yet non adhesive liquid embolic agent consisting of ethylene vinyl alcohol copolymer (EVAC) dimethylsulfoxide (DMSO), and tantalum powder
 - Once injected into bloodstream, DMSO diffuses away and EVAC precipitates radially from outside in leaving a soft non adherent mass that causes vascular occlusion
 - Approved by FDA in 2005 for preoperative embolization of AVMs

TUMOR EMBOLIZATION

- Onyx may be used **“off label”** to treat a variety of vascular pathologies including vascular tumors such as:
 - Metastases
 - squamous cell carcinoma
 - renal cell carcinoma
 - melanoma
 - multiple myeloma
 - Primary lesions
 - meningioma
 - osteosarcoma
 - hemangiopericytoma
 - choroid plexus papilloma
 - juvenile nasopharyngeal angiofibroma (JNA)
 - hemangioblastoma

HOW IS SUCCESSFUL EMBOLIZATION DETERMINED?

- It has traditionally been believed that the measure of a successful Onyx embolization of a tumor is visualization of angiographic penetration of Onyx into the tumor capillary bed as opposed to Onyx being visualized only in the feeding arterial pedicle.
- Some suggest 80% reduction in tumor blush indicates efficacy but this can be achieved with arterial pedicle embolization only without tumor penetration and therefore not be effective at the time of resection

WHAT DO THESE MEASURES MEAN?

- Elhammady MS, et al. J Neurosurg. 2010.
 - Percentage of devascularization may not be significantly different between tumors with and without angiographic intraparenchymal penetration (penetration may not be needed??)
- Rangel-Castilla, L. J Neurointerv Surg. 2012.
 - Utilized direct tumoral puncture and Onyx embolization if intraparenchymal penetration not seen during angiographic embolization

STUDY PURPOSE

- Hypotheses:
 - Preoperative transarterial embolization with Onyx may result in deep histologic tumor penetration even when deep penetration is not seen on angiography.
 - Angiographic findings do not predict degree of embolic penetration
- Method:
 - Compare angiographic and histologic penetration of Onyx in cases of transarterial embolization

STUDY DESIGN

- Preoperative embolization w/ Onyx 18
- Extent of devascularization objectively studied using computer software that compared a tumor's contrast opacification prior to and immediately after Onyx embolization.
- Angiograms subjectively evaluated for degree of tumor penetration
 - Good penetration: Onyx angiographically visualized in primary feeding vessel and tumor capillary bed
 - Poor penetration: Onyx not angiographically visualized in tumor bed

STUDY DESIGN

- Histologic evaluation of tumor following resection by an experienced surgical pathologist.
- Vascular penetration characterized after microscopic review as:
 - Central penetration: Onyx in the intratumoral vasculature
 - Peripheral penetration: Onyx only located within the interface of the lesional tissue with the background tissue or only within the lesion's capsule
 - Absent: No Onyx visible in the specimen

STUDY MATERIAL

- 22 patients (2009 – 2011; NONE LOST TO FU)
- All surgery within 72 hour of embolization
 - 17 head and neck + 5 spinal tumors
 - JNA 10
 - Meningioma 2
 - Plasma cell tumor 2
 - Renal cell met 2
 - Choroid plexus papilloma 1
 - Hemangiopericytoma 1
 - Capillary hemangioma 1
 - Osteosarcoma 1
 - Cerebellar hemangioblastoma 1
 - Squamous cell carcinoma 1

RESULTS

- Smallest vessel diameter penetrated (29um; 0.029mm)
- Onyx 18 used in all tumors. Onyx 34 used in one tumor to form initial proximal vascular plug to aid in embolization.
- Angiographic embolization (subjective evaluation)
 - Good 41%
 - Poor 59%
- Mean percentage angiographic devascularization 85.3% (using objective pixel evaluation software)
 - Percentage of objective devascularization did not correlate with subjective evaluation of angiographic Onyx penetration
 - Patients with Good subjective angiographic penetration had a mean objective devascularization of 78.1%
 - Patients with Poor angiographic subjective penetration had a mean devascularization of 90.3% (may be due solely to pedicle or feeding vessel sacrifice)

POSTOPERATIVE HISTOLOGIC EVALUATION

- Central penetration 59%
- Peripheral penetration only 32%
- No penetration 9%

HISTOLOGIC AND ANGIOGRAPHIC FINDINGS

- Central histologic + Good angiographic 27%
 - Usual marker of an ideal result
- Central histologic + Poor angiographic 32%
 - Procedure goal achieved but not predicted by images
 - Perhaps due to inability of imaging to detect tantalum density
- Peripheral histol + Good angiographic 9%
 - Perhaps due to contrast staining of tumor tissue mimicking tantalum
 - Perhaps due to imaging (timing, exposure, etc)
- Peripheral histol + Poor angiographic 23%
 - Perhaps due to pedicle or proximal feeding vessel sacrifice
- No histol penetration + Good angio 4.5%
 - Perhaps due to contrast staining of tumor tissue mimicking tantalum
 - Perhaps due to imaging (timing, exposure, etc)
- No histol penetration + No angio penetr 4.5%
- **TAKE AWAY MESSAGE: NO RELATIONSHIP BETWEEN SUBJECTIVE EVALUATION OF ANGIOGRAPHIC ONYX PENETRATION AND HISTOLOGIC PENETRATION ($p = 0.82$)**

HISTOLOGIC PENETRATION AND RADIOGRAPHIC DEVASCULARIZATION (PIXEL STUDY)

- 13 tumors with deep central penetration of Onyx into tumor had 84.3% radiologic devascularization
- 7 tumors with only peripheral penetration of Onyx into tumor had 84.8% radiologic devascularization
 - Possibly due to proximal occlusion of feeding vessels
- 2 tumors with no penetration of Onyx into tumor had 93.8% radiologic devascularization
 - possibly due to pure pedicle occlusion
- **TAKE AWAY MESSAGE: DEGREE OF HISTOLOGIC PENETRATION DOES NOT CORRELATE WITH RADIOGRAPHIC DEVASCULARIZATION AS EVALUATED USING PIXEL COMPARISON SOFTWARE**

CLINICAL FINDINGS

All surgery within 72 hours post embolization

- 77.3% within 24 hours
- 4.5% within 24-48 hours
- 18.2% within 48-72 hours

• Mean EBL 1342 ml

- Good angio penetration mean EBL 1151 ml
- Poor angio penetration mean EBL 1475 ml
- Central histologic Onyx penetration mean EBL 1079 ml
- Peripheral histologic Onyx/no Onyx mean EBL 1723 ml

– **TAKE AWAY MESSAGE: GOOD ANGIO PENETRATION AND CENTRAL HISTOLOGIC PENETRATION ARE PREDICTORS OF LOWER BLOOD LOSS (FORMER IS PROSPECTIVE AND LATTER IS RETROSPECTIVE AS IT RELATES TO SURGICAL PLANNING AND ANALYSIS)**

CLINICAL FINDINGS

- The percentage of tumor (pixel software determined) devascularization did not predict EBL regardless of angiographic penetrance.
- No difference in surgery time with good vs poor angiographic penetrance.
- Procedure related transient neurologic complications 1/22 (4.5%)

CONTEXT WITH PRIOR ONYX STUDIES

- Gobin YP. Radiology. 2001
 - 14 patients with head and neck tumors
 - >95% devascularization in 8/14 (57%)
 - 2 transient neurologic deficits (14.3%)
- Gore P. Neurosurgery. 2008 (letter)
 - 10 patients with cranial and spinal tumors
 - *“Excellent penetration with no complications”*
- Elhammady MS. J Neurosurg. 2010.
 - 34 patients
 - 85.4% mean devascularization in 18/34 (53%)
 - No complications
- Horowitz M, et al. (current study in press)
 - 85.3% mean devascularization
 - 1 transient complication (4.5%)

CONCLUSION

TAKE AWAY MESSAGE #1: NO RELATIONSHIP BETWEEN ANGIOGRAPHIC (SUBJECTIVE OPERATOR JUDGED) ONYX PENETRATION AND HISTOLOGIC (PATHOLOGIST DETERMINED) PENETRATION ($p = 0.82$)

TAKE AWAY MESSAGE #2: DEGREE OF HISTOLOGIC PENETRATION DOES NOT CORRELATE WITH RADIOGRAPHIC DEVASCULARIZATION AS EVALUATED USING PIXEL COMPARISON SOFTWARE (OBJECTIVE SOFTWARE JUDGED)

TAKE AWAY MESSAGE #3: GOOD ANGIO (SUBJECTIVE) PENETRATION AND CENTRAL HISTOLOGIC PENETRATION (OBJECTIVE) ARE PREDICTORS OF LOWER BLOOD LOSS (FORMER IS PROSPECTIVE AND LATTER IS RETROSPECTIVE AS IT RELATES TO SURGICAL PLANNING AND ANALYSIS)

TAKE AWAY MESSAGE #4: THE PERCENTAGE OF TUMOR (OBJECTIVE PIXEL SOFTWARE DETERMINED) DEVASCULARIZATION DID NOT PREDICT EBL

TAKE AWAY MESSAGE #5: THE LACK OF THESE ASSOCIATIONS CALLS INTO QUESTION THE USEFULNESS OF AN INTERVENTIONALIST'S JUDGMENT REGARDING ANGIOGRAPHIC DEVASCULARIZATION OR A COMPUTER SOFTWARE'S EVALUATION OF PIXILATION CHANGES AS PRESURGICAL ARBITERS OF EMBOLIZATION SUCCESS WHEN USING ONYX AS A TUMOR EMBOLIC AGENT

TAKE AWAY MESSAGE #6: NO DIFFERENCE IN SURGICAL TIME BETWEEN GOOD VS. POOR SUBJECTIVE ANGIOGRAPHIC PENETRANCE OF EMBOLIC AGENT

TAKE AWAY MESSAGE #7: EMBOLIZATION IS SAFE WITH 4.5% TRANSIENT NEUROLOGIC DEFICIT RATE