Embolic agents relevant to interventional neuroradiology

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Purpose

- To familiarize with the
  - Physical – chemical properties
  - behavior
  - Advantages and drawbacks
  - Risks
  - Indications and contraindications

Of embolic materials used in neuro-embolizations

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Goal of embolization

- To occlude pathological sections of the vascular tree
  - By physically blocking the target vessel using
    - Particles
    - Solidifying liquids

    embolization
  - By inducing thrombosis:
    - Sclerotizing agents

Clinical goals

- Preoperative embolization:
  - To assist surgical removal of vascular lesions
    - To make surgical manipulation easy and less traumatic
    - To reduce lesion size:
      - By inducing tissue necrosis (tumors)
      - By reducing pulsatility (AVMs)
    - To reduce blood loss
    - to reduce surgical risk
  - To assist radiosurgery:
    - to reduce lesion size to make targeted irradiation effective (???)

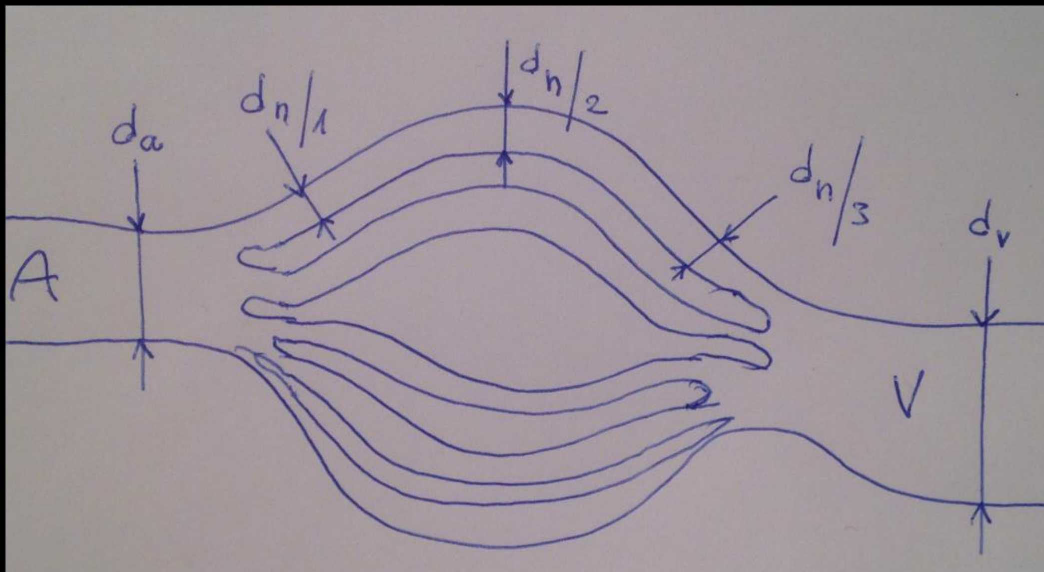
Clinical goals

- To cure vascular lesions:
  - By complete occlusion of AVM nidus
- Palliative treatment:
  - Partial targeted embolization of malformations
  - To stop tumor growth by embolization without surgical removal

Choice of embolic material

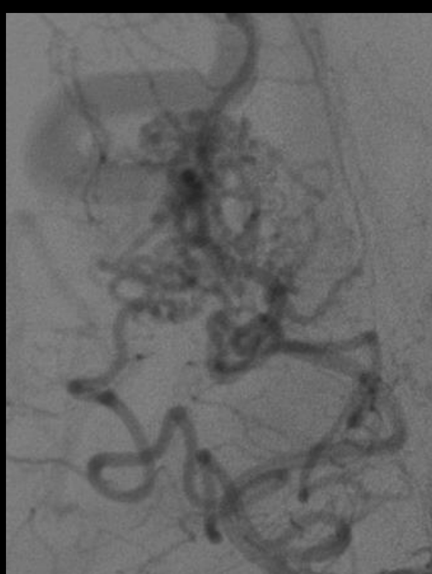
- Needs to be selected
  - In relation to the clinical goal
  - In relation to the morphological features of the vascular section to be embolized

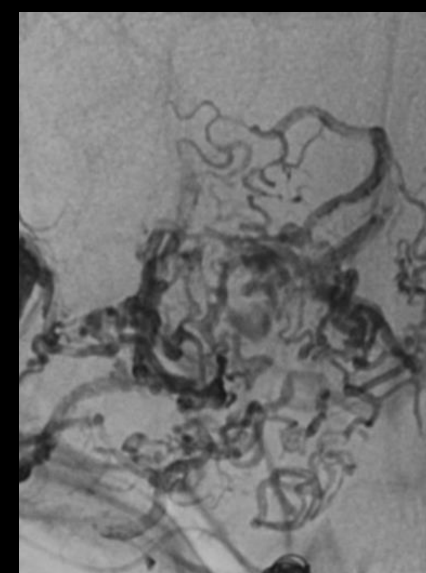
Patho-morphological considerations: AVM



$D_n \leq D_a$

$D_n/1 = D_n/2 = D_n/3$





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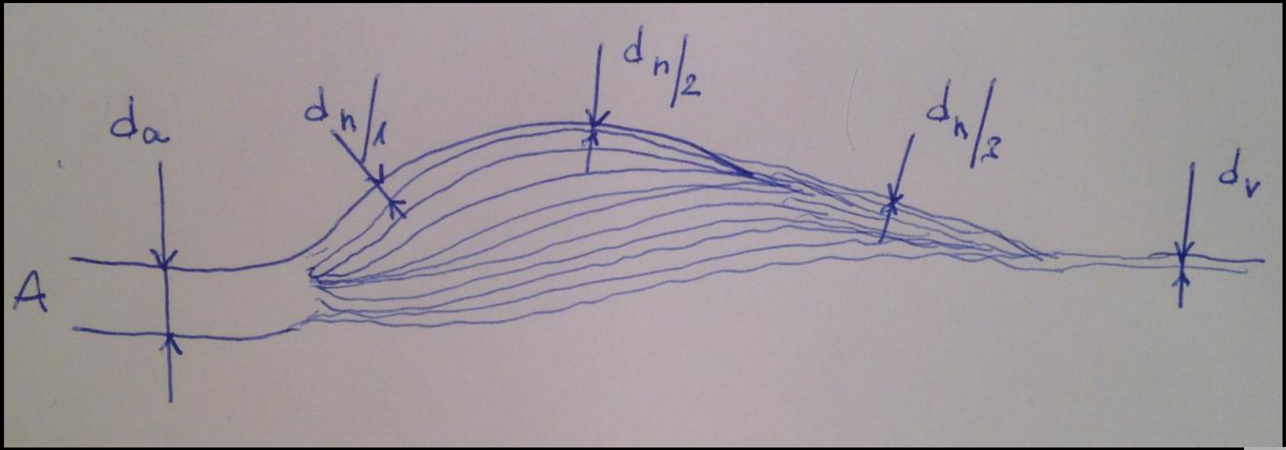
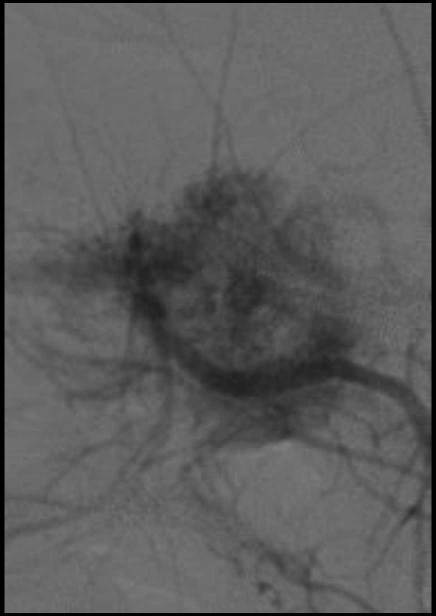
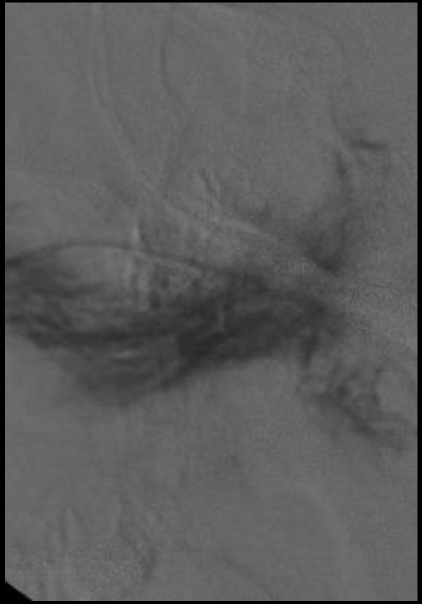
Patho-morphological considerations: tumors

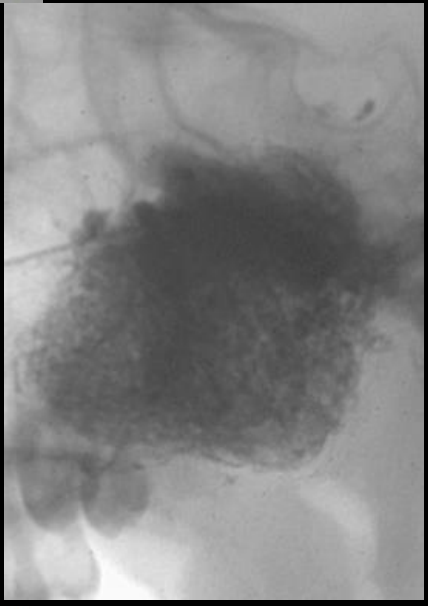


$D_n <<< D_a$

$D_n/1 > D_n/2 > D_n/3$







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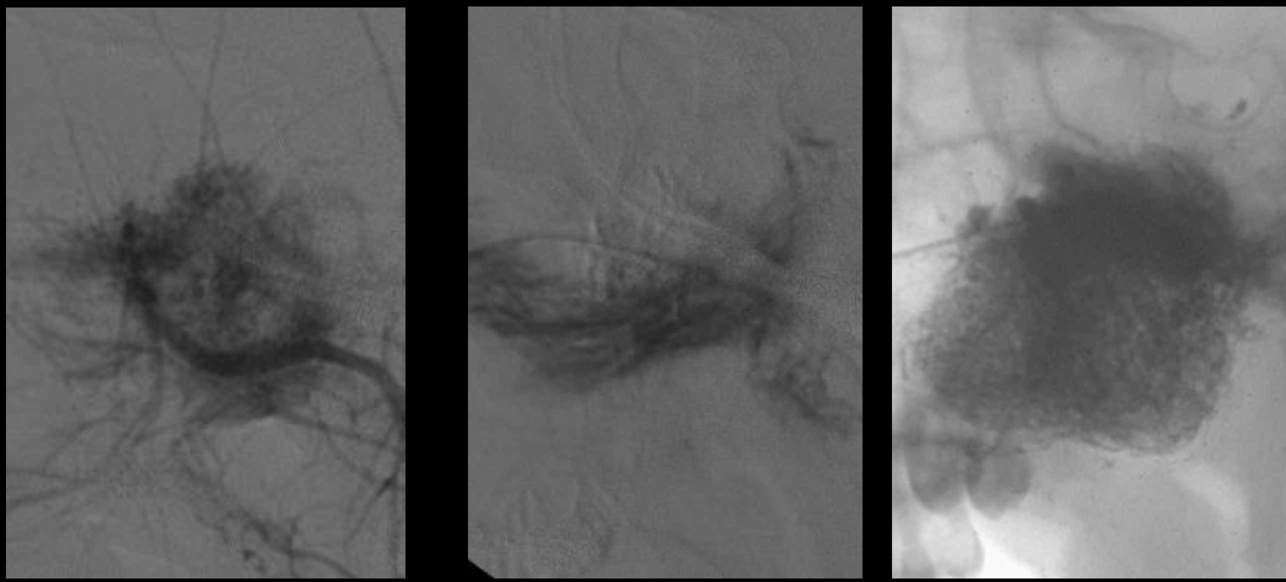
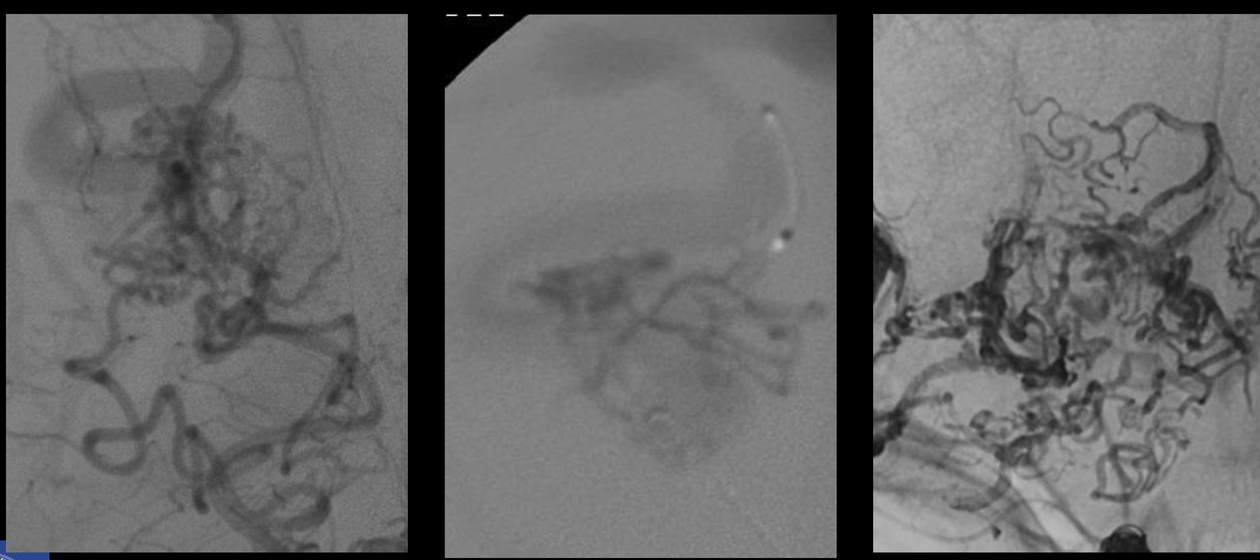
Patho-morphological considerations

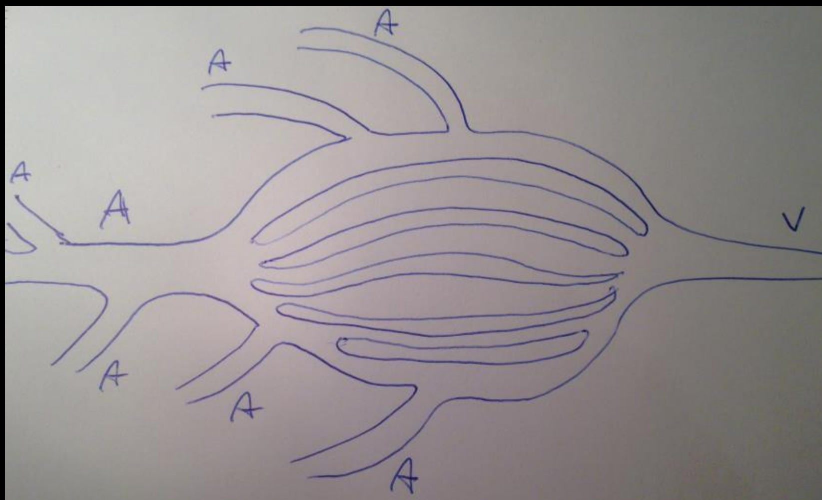


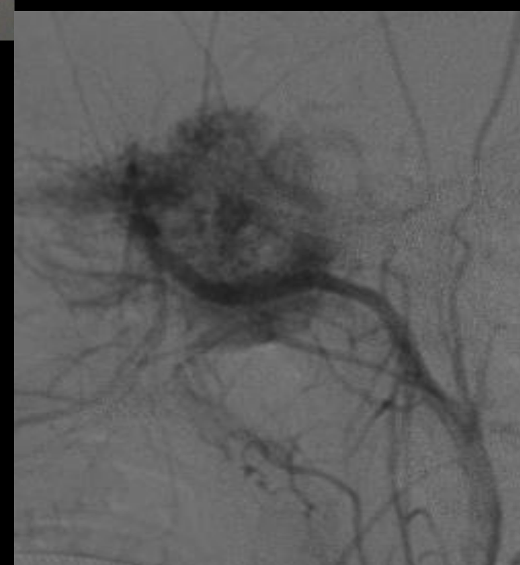
Tumors:
blocking the vascular bed with particles is possible

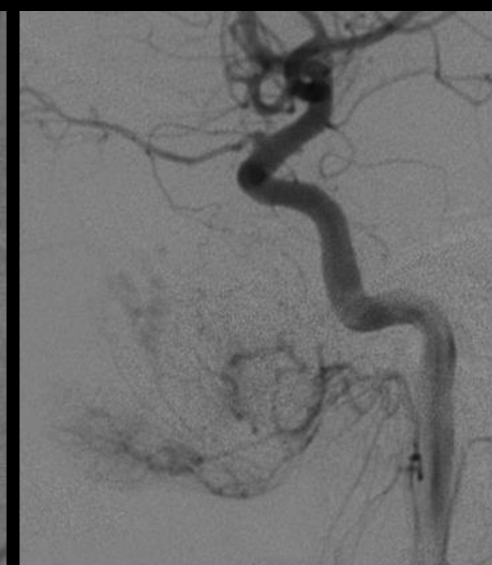


AVMs:
blocking the nidus with particles is difficult/impossible

Patho-morphological considerations







- Multiple feeding pedicles supplying nidus/tumor bed
- Proximal feeder occlusion is useless in both tumors and AVMs

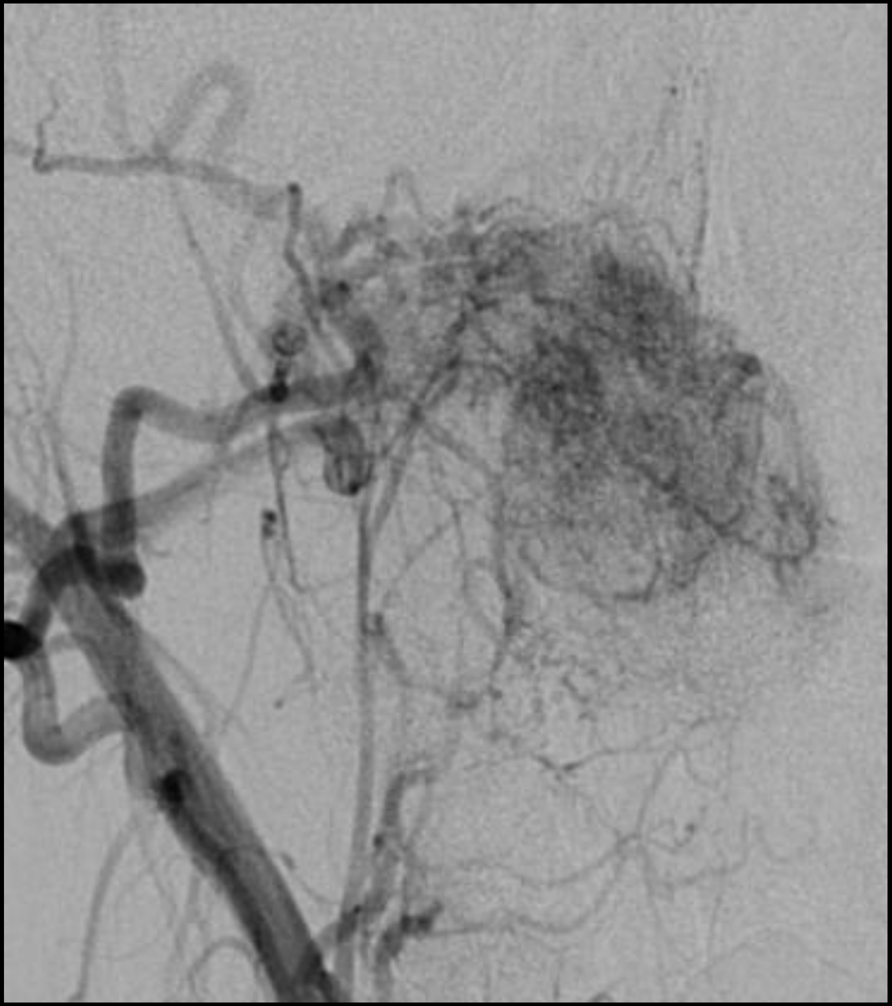
Embolic particles

- Prerequisites:
  - Selection of sizes shopuld be available for the
    - for the particular anatomy
  - Non-resorbable material
  - Non toxic
  - Visible by fluoroscopy

Available choices: Polyvinyl alcohol (PVA)

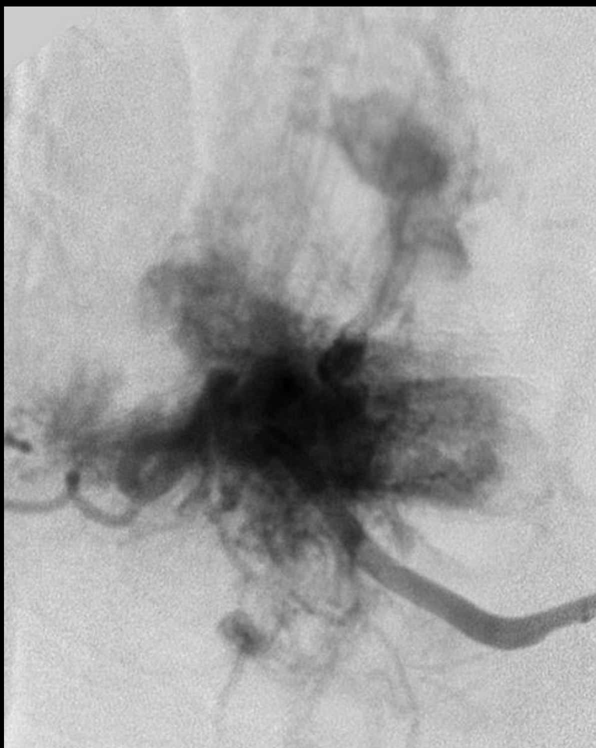
- Most frequently used in neurointerventions
- Available in large size range (50-1200μ)
  - Distal tumor bed embolization: 50-150μ
  - Proximal occlusion: 150-300μ
- Advantage:
  - Easy to handle
  - Cheap
  - Effective for preoperative tumor embolization (only)

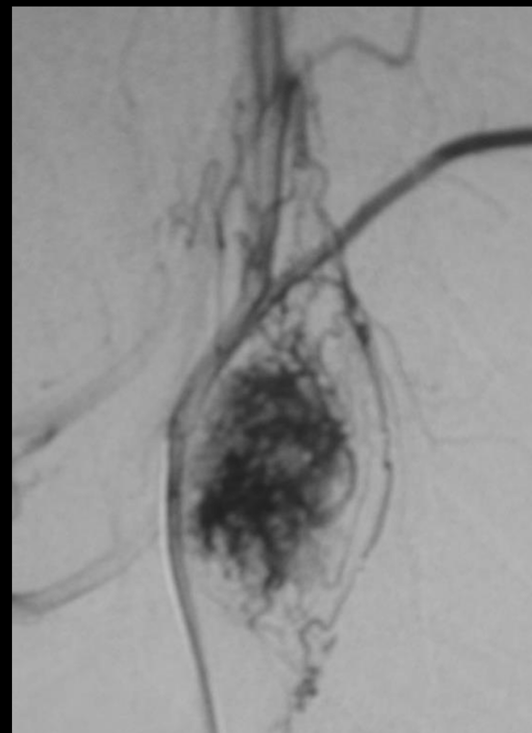
Polyvinyl alcohol (PVA)

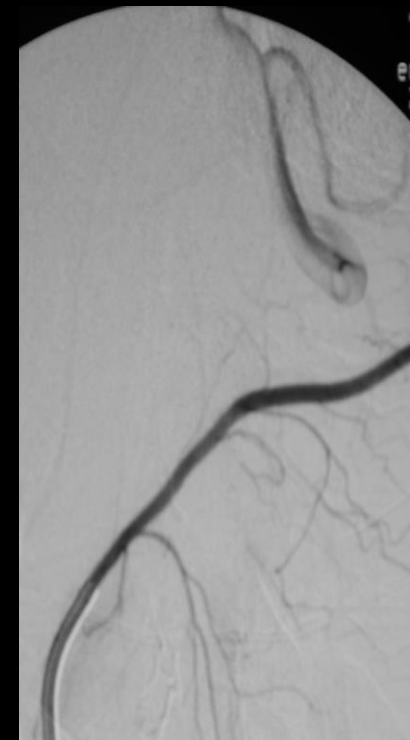


- To achieve deep penetration:
  - Small size (50-150μ)

Polyvinyl alcohol (PVA)







High flow shunts: Large size (350-500µ)

Dangerous anastomoses: large size (150-250µ)

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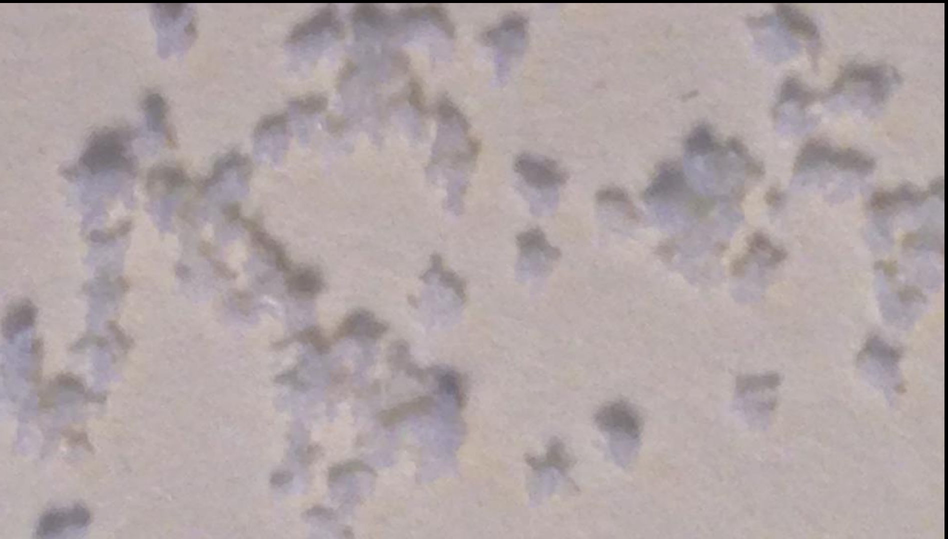
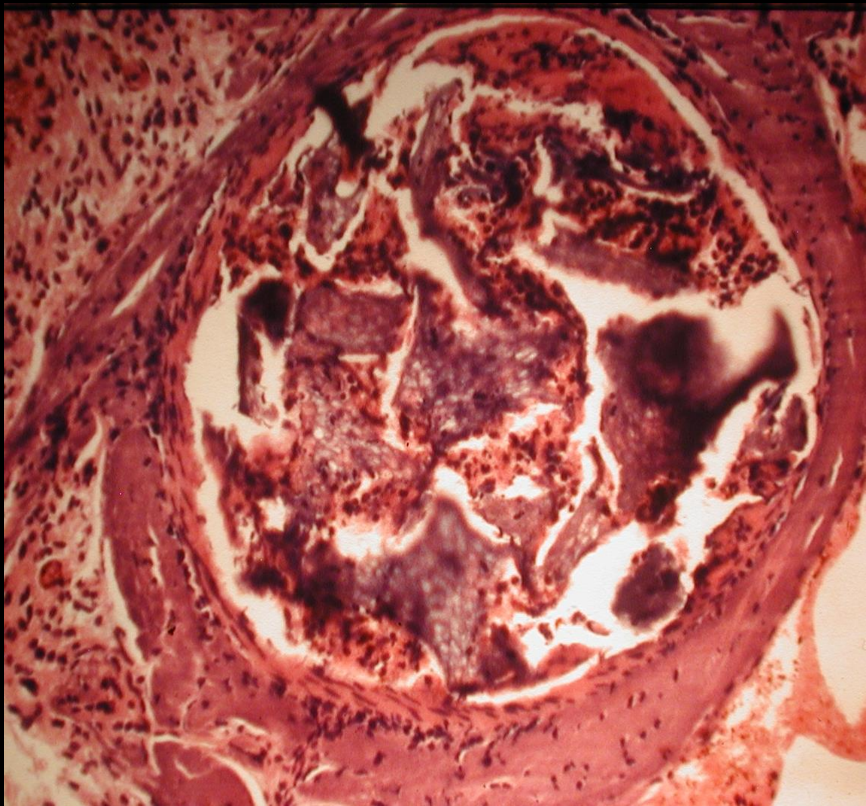
Polyvinyl alcohol (PVA)

- Disadvantages:
  - Irregularly shaped PVA flakes
  - Can clog the catheter
  - can not homogeneously block the target vessel
  - the plug will consist of mixture of PVA and blood
  - Recanalization by resorption of blood clot
  - Surgery needs to be done in a few days



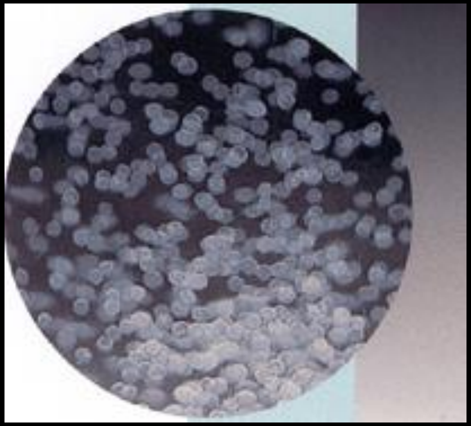


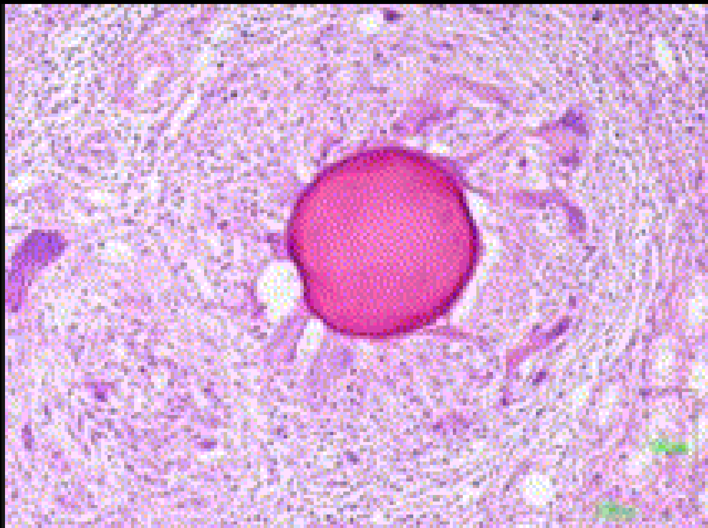
Polyvinyl alcohol (PVA)

- Disadvantages:
  - Non-radio-opaque:
    - Visualized by added contrast material
    - Particles are not visible
    - Inadvertent embolization into normal pedicles may remain unnoticed
  - Quickly sedimentates in solution

Trisacryl gelatin microspheres

- Collagen coated, hydrophilic, spherical
- Available in different sizes
- Advantages:
  – Lower risk of clogging the catheter
    - Hydrophilic, spherical
    - Homogeneous filling of vessel





Trisacryl gelatin microspheres

- Compressibility:
  - Up to 30% for easier passage through microcatheter
- Radio-opacity:
  - EmboGold:
    - impragneted by 2% Gold for visibility

Liquid embolics

- Purpose of using liquid agents:
  - Complete filling of the target vascular section
    - By creating a cast of the nidus/vascular bed
  - Reaching the draining vein through the nidus
  - To avoid recanalization through collateral channels feeding the nidus/vascular bed
- Solidification mechanisms:
  - Upon contact with blood
    - Polymerization
    - precipitation

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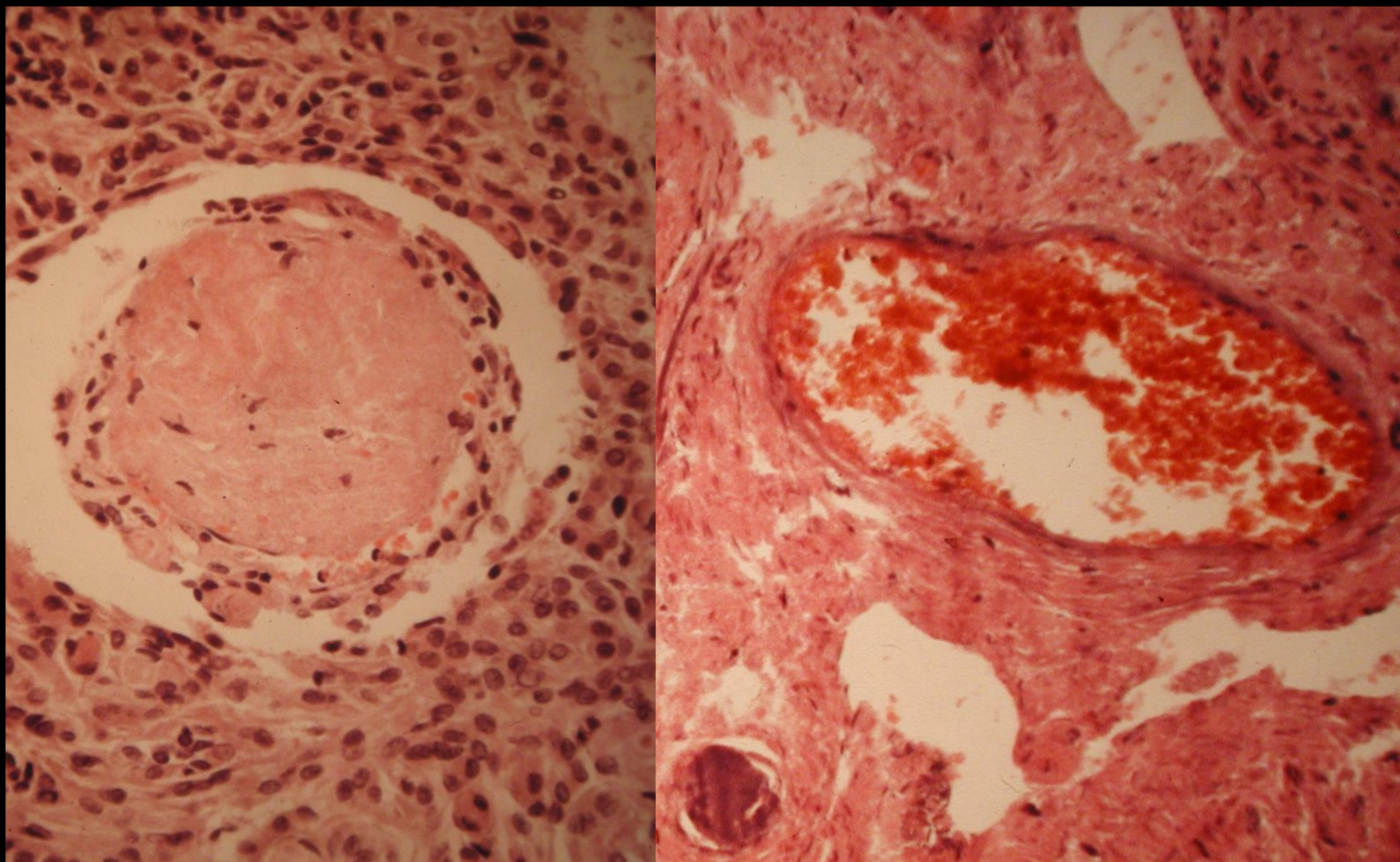
Liquid embolics

- Permanent occlusion if complete filling
- Recanalization is possible if partial filling



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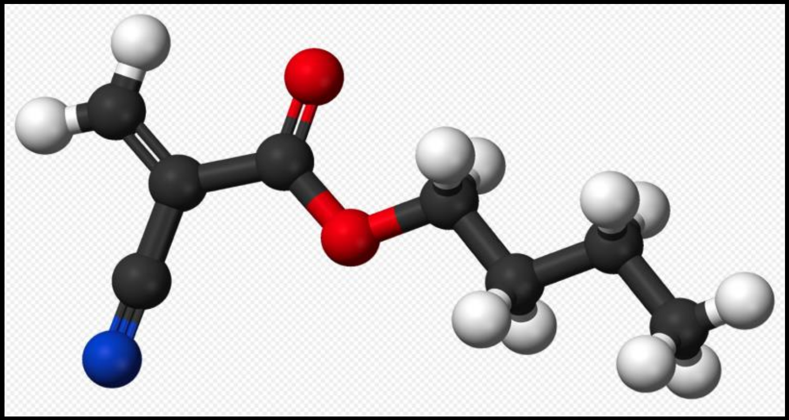
Tissue adhesives



- Thrombin glue (Tissucol):
  - Has been tested
  - Not used for low efficacy
- Cyanoacrylates:
  - Gold standard for decades
  - IBCA (Isobutyl 2-cyanoacrylate):
    - not used for embolization for carcinogenicity
  - NBCA (Butyl 2-cyanopropenoate, $C_8H_{11}NO_2$)
    - Cyanoacrylate ester
    - Widely used as tissue adhesive
  - Acting mechanism:
    - Quickly polymerizes in an ionic environment
    - Glubran (Europe), TrueFill (US)

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Cyanoacrylate glue

- Advantages:
  - Polymerization time can be individually adjusted
    - dilution of the glue with oil
    - Solidification time is related to glue concentration in the emulsion
  - Radio-opacity:
    - Can be achieved by
      - addition of metallic powder (Tantalum) if pure glue is used
      - Addition of oily contrast material (Iophendylate (=Lipiodol)

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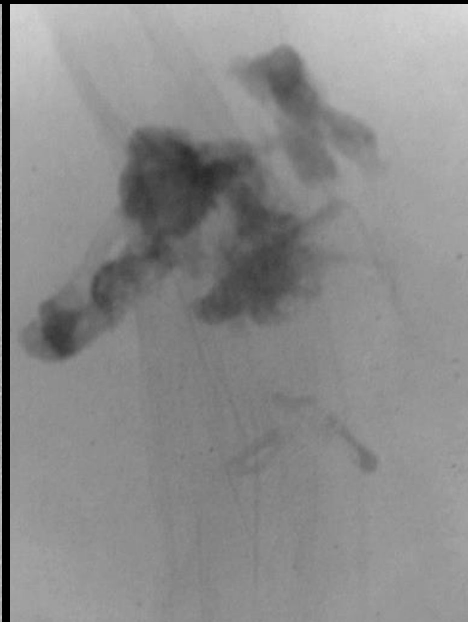
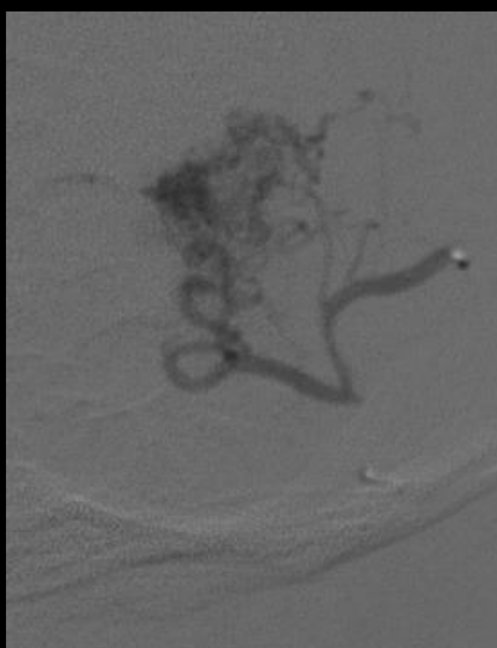
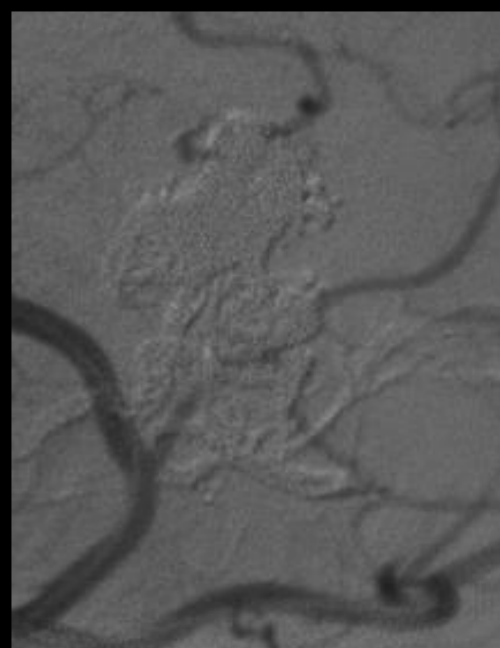
Cyanoacrylate glue



Direct fistula: low dilution / pure glue





Small vessels, proximal position: high dilution

Cyanoacrylate glue

- Disadvantages:
  - Highly adhesive
    - Injection time is limited
    - May get delivery catheter stucked
  - Lack of cohesiveness:
    - Injected glue may flow away in droplets
  - Thrombogenic:
    - May cause thrombosis in draining vein

Cyanoacrylates

- Disadvantages:
  - Rigid when polymerized
  - Makes surgical removal difficult
    - Difficult to cut
    - Not compressible (bleeding control)

Non-adhesive liquid embolics

- Purpose:
  - To improve penetration
    - To reach the vein through the nidus
  - To reduce the risk of glueing the microcatheter

Ethylen-vinylalcohol-copolymer (EVOH)

- Acting mechanism:
  - EVOH polymer is solved in an organic solvent (dimethyl-sulfoxid, DMSO)
  - DSMO is easily solved in blood
  - Upon contact with blood
    - DMSO diffuses into blood
    - EVOH solidifies by precipitation

Ethylen-vinylalcohol-copolymer (EVOH)

- Physical properties:
  - Non-adhesive
  - Highly cohesive
    - Solidifies on the surface:
      - Inner part remains liquid for relatively long
      - allows for penetration into different directions

Ethylen-vinylalcohol-copolymer (EVOH)

- Advantages:
  - Injection time is much less limited
    - Does not glue to microcatheter
    - Can be expanded almost without any limit by using detachable tip microcatheters
    - Allows for very deep penetration into nidus
    - Non thrombogenic
      - (even in the vein)

Ethylen-vinylalcohol-copolymer (EVOH)

- Advantages:
  - Softer, easier to cut

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Ethylen-vinylalcohol-copolymer (EVOH)

- Disadvantages:
  - Solidification time can not be individually modified
  - Microcatheter can get stuck by friction
    - Aggressive removal may cause rupture
    - Can be handled by detachable tip microcatheters
  - May cause bleeding
    - Because high efficacy –deep penetration
      - Unnoticed venous occlusion
  - DMSO is toxic:
    - Causes SAH in higher volume / fast injection
    - Provokes nausea/vomiting, headaches postprocedure

Ethylen-vinylalcohol-copolymer (EVOH)

- Radio-opacity:
  - Provided by added Tantalum powder
  - Needs thorough mixing – preparation time!
  - Tendency to sedimentate
  - Microcatheter is rinsed with DMSO
  - EVOH is diluted in microcatheter
  - First drops have low visibility

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Products

- ONYX ™ (Covidien Neurovascular)
  - Available in different concentrations:
    - 6-8% for different flow rates
- SQUID™ (Emboflu)
  - Smaller grain size of Tantalum
    - More homogeneous visualization
    - Less sedimentation
    - Different concentration and radio-opacity

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Other non-adhesive liquid embolics

- PHIL ™(Microvention): Precipitating Hydrophobic Injectable Liquid
  - Hydroxyethyl methacrylate (PHEMA)
  - Co-polymer dissolved in DMSO
  - Inherent radiopacity by covalently bonded Iodine
  - Non-thrombogenic
  - Less intense, homogeneous radio-opacity
    - No sedimentation
- EASYX:
  - Iodinated PVA (poli-vinyl alcohol) ester
  - Precipitating Polymer
  - Dissolved in DMSO
  - Homogeneous, lower radiopacity (intrinsic iodine)
  - No artifacts on CT
  - Awaiting for CE mark

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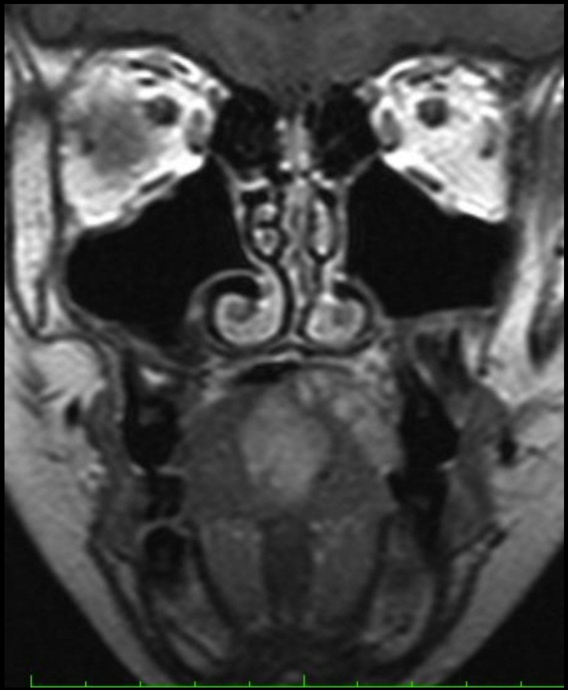
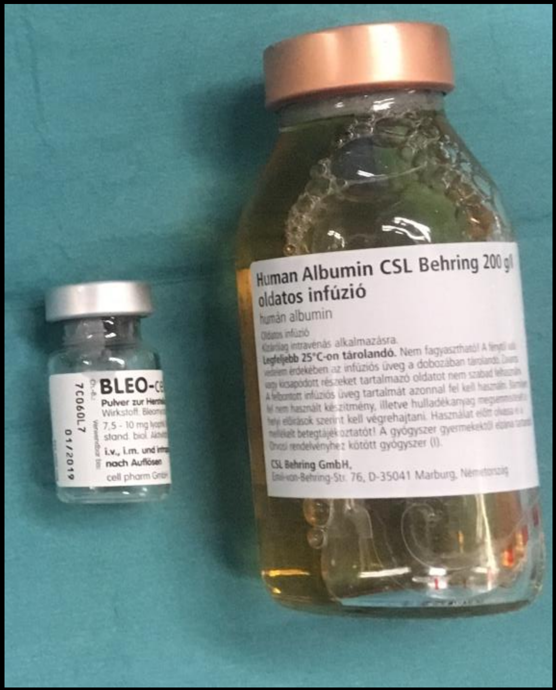
Sclerotising agents:

- Sclerotization is used for venous malformations (head and neck)
  - 96% ETOH:
    - Easy to use
    - Short action time in the target venous dilatation
    - Volume limited
      - High volume cause pulmonary hypertension (< 50% [in cc] of body weight [kg]!!!)
      - Non-visible
  - Jellified alcohol (ScleroGel TM):
    - Longer residence time in lesion
    - Visibility
  - Polidocamol (Ethoxysclerol)
  - Bleomycin

Sclerotising agents:

- Bleomycin:
  - Bleomoycin foam:
    - Bleomycin-20% Albumin-contrast material-air : 1:1:1:1
- Polidocamol (Ethoxysclerol)





Summary

- Particulate embolization
  - Capable for preoperative tumor embolization
- Liquid embolics:
  - Adhesives: cyanoacrylates
  - Non-adhesives:
    - EVOH
    - Other materials (PHIL, HELP)
    - Used for permanent embolization
- Sclerotizing agents:
  - Exclusivey used for venous malformations