Liquid embolization of HCC

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Disclosure

Speaker name:

Pr Romaric LOFFROY

I have the following potential conflicts of interest to report:

☒ Consulting: Medtronic, Balt, Guerbet, GEM
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☐ I do not have any potential conflict of interest
When to use liquid embolics for HCC?

- Chemo-embolization
  - Conventional TACE (cTACE)
- Lipiodol tattoo
  - Before thermal ablation
- Portal vein embolization
  - Before hepatectomy (FLR)
- Hemostatic embolization
  - HCC rupture

Lipiodol +++

NBCA +++
Place of TACE in the BCLC
cTACE: what have we learned?

- cTACE must be used in HCC selectively targetable & accessible to supraselective catheterization
  - To improve outcomes
  - To maximize the anti-tumoral effect
  - To minimize the collateral damages of the surrounding liver parenchyma

EASL Clinical Practice Guidelines. J Hepatol 2018
ESMO Clinical Practice Guidelines. Ann Oncol 2018
cTACE technique standardization

- Superselective cTACE (ss-cTACE)
- < 2.0-Fr microcatheter
- Ideally < 5 lesions, ≤ 2 segments, < 5 cm
- Use of angio-CBCT
- Whole tumor should be covered
- Adding peritumoral margins is encouraged
- Treatment should involve a water-in-oil emulsion
- Additional particulate embolization should be systematically performed
- Non-contrast CBCT or MDCT combined with angiography should be systematically used to assess the tumor coverage

Loffroy et al. Radiology 2013
De Baere et al. CVIR 2022
Lipiodol tattoo

3 HCCs: II, VII, V
ss-TACE in 1 session
MWA the day after in 1 session
PVE: NBCA is the gold standard

- As compared to other embolic agents
  - Greater & faster liver growth
  - Lower radiation dose
  - Cheaper
  - No more complications

Properties
- Fast polymerization & highly adhesive & hepatic inflammation

Potential drawbacks
- Risk of non-target vessel embolization
- Risk of catheter adherence
- Low delivery control which needs expertise

Loffroy et al. Curr Vasc Pharmacol 2009
Denys et al. CVIR 2010
Hill et al. Diagn Interv Radiol 2018
Wajswol et al. CVIR 2018
Mendes Luz et al. Radiology 2021
## Cyanoacrylates: types & actions

<table>
<thead>
<tr>
<th></th>
<th>Methyl</th>
<th>Butyl</th>
<th>Hexyl</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NMCA</strong></td>
<td>SuperGlue®</td>
<td>NBCA</td>
<td>NBCA + CM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Histoacryl®</td>
<td>Glubran®2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trufill®</td>
<td></td>
</tr>
<tr>
<td>CH3 radical</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Polymerization time</td>
<td>Very fast</td>
<td>Fast</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Cytotoxicity</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Inflammation</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Adhesive strength</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
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</tbody>
</table>
PVE technique

• General anesthesia
• Ipsilateral/contralateral approach under US guidance
• 5-Fr introducer sheath inserted into the portal vein
• Portography 3D/CBCT with 4-Fr catheter
• Use of a microcatheter may be useful
• Embolization of portal targeted vein under fluoroscopic guidance from distal branch by reflux
• Final portography
• Liver track embolization with gelfoam
Mixture of glue & lipiodol

• Previous catheter flushing with dextrose 5%

• Mixing with Lipiodol® (Guerbet)
  • Makes the mixture radiopaque
  • Modulates the rate of polymerization
  • Plastic 3-way stopcock
  • Non polycarbonate luer-locked syringes
  • 1:8 ratio

• Slow & regular injection of glue/Lipiodol® mixture under fluoroscopy
  • Free-flow injection
    • One-shot
  • No rush with catheter withdrawn
  • Pull out curtly the catheter after getting your goal
  • Avoid doing ‘that little bit more’ just to make the final result look better

Mixture ready to inject
Meta-analyses

• CVIR 2018
  • 1970 to 2018
  • 18 papers
  • 607 patients (89 HCC)
  • Technical success 99.3%
  • Hypertrophy rate of the FLR 49.4%
  • Surgical resection rate 75.9%
  • Complications
    • Major 3.1%
    • Minor 6.3%

• Eur Radiol 2021
  • 1998 to 2019
  • 51 papers
  • 2896 patients (61% treated with NBCA or particles)
  • NBCA vs particles
    • Hypertrophy FLR
      • 49.1 vs 42.2% (p=0.037)
    • Complications
      • 4 vs 5% (p>0.05)
    • Procedural time
      • 215 vs 348 min (p<0.001)
    • Radiation dose
      • 573 vs 1287 Gycm² (p<0.01)
    • Cost
      • 816 vs 4233 € (p<0.0001)
BestFLR Trial: Liver Regeneration at CT before Major Hepatectomies for Liver Cancer—A Randomized Controlled Trial Comparing Portal Vein Embolization with N-Butyl-Cyanoacrylate Plus Iodized Oil versus Polyvinyl Alcohol Particles Plus Coils

José Hugo Mendes Luz ¹, Filipe Veloso Gomes ¹, Nuno Vasco Costa ¹, Inês Vasco ¹, Elia Coimbra ¹, Paula Mendes Luz ¹, Hugo Pinto Marques ¹, João Santos Coelho ¹, Raquel Maria Alexandre Mega ¹, Vasco Nuno Torres Vouga Ribeiro ¹, Jorge Tiago Rodrigues da Costa Lamelas ¹, Maria Mafalda de Sampaio Nunes E Sobral ¹, Silvia Raquel Gomes da Silva ¹, Ana Sofia de Teixeira Carrelha ¹, Susana Cristina Cardoso Rodrigues ¹, António Augusto Ferreira Pinto de Figueiredo ¹, Margarida Varela Santos ¹, Tiago Bilhim ¹

group (P = .27). Conclusion Portal vein embolization with N-butyl-cyanoacrylate plus iodized oil produced greater and faster liver growth as seen at CT in participants with liver cancer, compared with portal vein embolization with polyvinyl alcohol particles plus coils, allowing for earlier surgical intervention. © RSNA, 2021 Online supplemental material is available for this article. See also the
What about EVOH?

- No randomized trial available comparing liquids
- Our experience of PVE with EVOH
  - Technical success rate = 100%
  - Clinical success rate = 100%
  - No major complications
    - Only 4 mild post-embolization symptoms treated by acetaminophen
  - $DH = 16.7 \pm 6.7$
  - $% \text{FLRV} \text{increase} = 52.9 \pm 32.5\%$
  - $\text{KGR} = 4.4 \pm 2.0\%$
  - 84.5 % surgical resection rate

EVOH dissolved in dimethyl sulfoxide (DMSO)

**Properties**
- Cohesive, nonadhesive
- High radio-opacity
- Micronized tantalum powder
- Slow solidification rate
- High delivery control
## Reported literature

<table>
<thead>
<tr>
<th>Embolization material</th>
<th>Article</th>
<th>N</th>
<th>% increase FLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrin glue</td>
<td>Liem</td>
<td>15</td>
<td>31.4</td>
</tr>
<tr>
<td></td>
<td>Nagino</td>
<td>105</td>
<td>27.4</td>
</tr>
<tr>
<td>N-butyl cyanoacrylate</td>
<td>Wajswol (meta-analysis)</td>
<td>607</td>
<td>49.4</td>
</tr>
<tr>
<td>Gelatin sponge</td>
<td>Fujii</td>
<td>30</td>
<td>17.8</td>
</tr>
<tr>
<td></td>
<td>Makuuchi</td>
<td>54</td>
<td>37.9</td>
</tr>
<tr>
<td></td>
<td>Nanashima</td>
<td>30</td>
<td>29.4</td>
</tr>
<tr>
<td></td>
<td>Sugawara</td>
<td>66</td>
<td>35.8</td>
</tr>
<tr>
<td>PVA + coils/vascular plugs</td>
<td>Libicher</td>
<td>10</td>
<td>26.4</td>
</tr>
<tr>
<td></td>
<td>Guiu</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>STS</td>
<td>Fischman</td>
<td>35</td>
<td>48.8</td>
</tr>
<tr>
<td>Onyx</td>
<td>Our study</td>
<td>26</td>
<td>52.9</td>
</tr>
</tbody>
</table>

Laffroy et al. QIMS 2021
In some situations

• PVE and Onyx®

1. 2018: during PVE with NBCA, EVOH has been found useful for occluding portal vein branches for which the use of NBCA was deemed to carry a high risk of non-target embolization

2. 2019: in a study of 41 patients, EVOH used in 11 patients, produced faster growth of the S2/3 segments compared to ethiodized oil (n=10), polyvinyl alcohol (n=8), and ligation (n=12)

MAIN CHARACTERISTICS OF PVE USING NCBA AND ONYX

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Embolic agent</th>
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<tbody>
<tr>
<td></td>
<td>Onyx</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>Mandatory</td>
</tr>
<tr>
<td>Preparation time</td>
<td>15 min</td>
</tr>
<tr>
<td>Delivery control</td>
<td>Easy</td>
</tr>
<tr>
<td>Adhesiveness</td>
<td>No</td>
</tr>
<tr>
<td>Radio-opacity</td>
<td>Very high</td>
</tr>
<tr>
<td>Non target embolization</td>
<td>Less risky</td>
</tr>
<tr>
<td>Time to occlusion</td>
<td>Solidification in 5 min</td>
</tr>
<tr>
<td>Vessel occlusion</td>
<td>Complete &amp; permanent</td>
</tr>
<tr>
<td>Recanalisation</td>
<td>Low</td>
</tr>
<tr>
<td>Inflammatory reaction</td>
<td>Medium</td>
</tr>
<tr>
<td>Cost</td>
<td>Expensive</td>
</tr>
<tr>
<td>% increase FLR</td>
<td>52.9</td>
</tr>
</tbody>
</table>

Breguet et al. Eur Radiol 2018
Biggemann et al. MITAT 2019
Hemostasis with glue for HCC rupture

52 yo male
Nodular HCC rupture
Healthy liver
Hemodynamically unstable
Superselective embolization with Glubran® 2
Ratio NBCA/Lipiodol 1:5
Theoretical advantages

- Permanent, no recanalization
- Highly penetrable
- Occlusive effect does not depend on coagulation parameters
- High hemostatic effect
- Interesting for massive bleeding
- High radiopacity
- Can reach distal targets that cannot be navigated with catheters
- Easy to deliver
- Free or blocked flow
- Best options with neuro microcatheters
Complete response at 2 months on MRI
Then wedge resection
Still alive with no recurrence at 5 years!
Conclusion

• Liquid embolics can be used at all stages of treatment of HCC
  • To treat the tumor
    • cTACE
  • To tattoo the lesion
    • Before ablative techniques
  • To induce liver hypertrophy
    • Before hepatectomy
  • To stop the bleeding
    • In case of HCC rupture