Guerbet

STANDARDIZATION IS KEY FOR REPRODUCIBLE AND OPTIMAL cTACE PROCEDURE

References

«For 30 years, Lipiodol® TACE has been inconsistently referenced in many publications with various levels of details for the method of preparation and administration, with reported progressive outcomes following improvements in the technique and the devices used to deliver the treatment and better patient selection. Consequently, there is no consensus on the standard method of TACE regarding the use of anticancer agents, embolic material, technical details, and the treatment schedule. In order to develop an internationally validated technical recommendation to standardize the Lipiodol® TACE procedure, a worldwide panel of experts participated in a consensus meeting held on May 10, 2014[1,2].»

DEFINITION AND RATIONALE

What is cTACE standardization?

- cTACE standardization consists in preparing the anticancer agent in a water-in-oil emulsion before administration[1].
- *«It has been widely demonstrated that a water-in-oil emulsion made of droplets is more densely retained within the tumors than the alternative oil-in-water emulsion[2].»*

Why cTACE must be standardized?

- cTACE must be standardized to get better results during and after the procedure. This means that the procedure must be prepared with consistency and reproducibility.
- *«The standardization of this procedure allows to perform cTACE in a more efficient and safer way. Indeed, the water-in-oil emulsion (Lipiodol® Ultra Fluid/drug), followed by the embolization particles will allow an improvement of the pharmacokinetics of the drug, but also a better tumor response[2].»*

What are the endpoints of this procedure?[1]

- Drug/Lipiodol® Ultra Fluid oil emulsion type (W/O).
- Volume of drug aqueous solution/Volume of Lipiodol® Ultra Fluid.
- Number of pumping exchanges between Lipiodol® Ultra Fluid & drug.

A two-step procedure

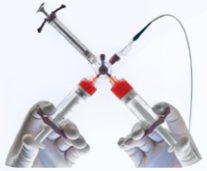
I. MIXTURE PREPARATION

II. ADMINISTRATION OF EMBOLIC MATERIAL

Materials to perform the procedure

- **Lipiodol® Ultra-Fluid,** 480 mg Iodine/mL, solution for injection.

- **Vectorio®:** Lipiodol® Ultra Fluid resistant mixing and injection system for conventional Trans-Arterial Chemoembolization (cTACE).



- **Anticancer agents:** doxorubicin[1], miriplatin[3], epirubicin[3], cisplatin[4], mitomycin[5].
- **Embolic material:** Gel-Foam or Embolic particles.

Vectorio® IFU

Lipiodol® Ultra Fluid SmPC

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- Drug/Li…
- Volume …
- Number of pumping exchanges between Lipiodol® Ultra Fluid & drug.

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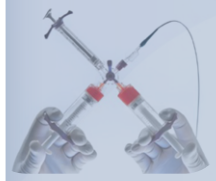

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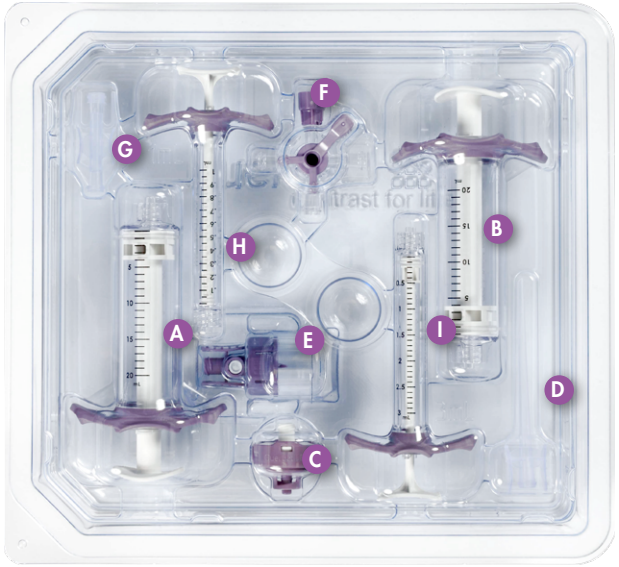
…lic particles.

VECTORIO® COMPOUNDS

Raw materials of Vectorio® have been validated for resistance to Lipiodol® Ultra Fluid up to 24h.



- A & B 20 mL mixing syringes (x2)
- C Particle filter for Lipiodol® Ultra Fluid withdrawal (x1)
- D Lipiodol® Ultra Fluid ampule withdrawing straw (x1)
- E *Lipiodol® Ultra Fluid vial spike (x1)
- F 3-way stopcock with 4 connections (x1)
- G Connector (x1)
- H 1 mL injection syringe (x1)
- I 3 mL injection syringe (x1)

The system does not contain:

- Lipiodol® Ultra Fluid ampule or vial
- Anticancer drug
- Microcatheter

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PROCEDURE

KEY GOLDEN RULES FOR AN OPTIMAL STANDARDIZATION PROCEDURE IN cTACE: MIXTURE PREPARATION & ADMINISTRATION OF EMBOLIC MATERIAL

I. MIXTURE PREPARATION: 4 STEPS

1

Prepare a syringe containing Lipiodol® Ultra Fluid and a syringe containing the anticancer agent

Prepare the mixture using Vectorio® SET :

- Withdraw Lipiodol® Ultra Fluid from ampoule using 20ml mixing syringe and filter+straw;
- Withdraw anticancer drug from containing syringe, using 20ml mixing syringe and connector.

Recommended

- Anticancer agents: doxorubicin[1], miriplatin[3], epirubicin[3], cisplatin[4], mitomycin[5]
- Ratio to follow: **1 drug volume to 2 Lipiodol® Ultra Fluid volumes**

IMPORTANT!

Caution

- **A maximum of 15ml Lipiodol® Ultra Fluid** can be administered to the patient
- Always maintain the **appropriate ratio** between anti-cancer drug and Lipiodol® Ultra Fluid

2

Connect both syringes to a three-way-four-port stopcock.

3

Mixing: anti-cancer drug should be first pushed towards the syringe containing Lipiodol® Ultra Fluid.

Water-in-oil emulsion[6]

- Use the three-way-four-port stopcock
- Vigorous mixing of Lipiodol® Ultra Fluid & anticancer drug: perform minimum **20 back & forth movements between the two syringes to obtain a homogeneous emulsion[1].**

Recommended

- The **quality of emulsion** should be assessed with a **"drop test"[2]**
  > Water-in-oil and oil-in-water

4

Obtention of an emulsion of Lipiodol® Ultra Fluid + anticancer agent drug.

You can now perform Super-Selective cTACE

With courtesy of Pr. Thierry De Baere.

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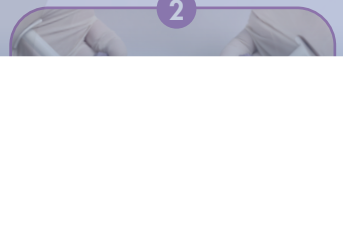
KEY GOLDEN RULES FOR AN OPTIMAL STANDARDIZATION PROCEDURE IN cTACE: MIXTURE PREPARATION & ADMINISTRATION OF EMBOLIC MATERIAL

I. MIXTURE PREPARATION: 4 STEPS

1

2



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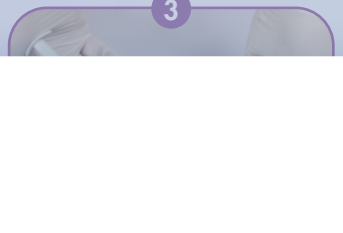

4

Prepare a syringe co
and a syringe contai

Prepare the mixture

- Withdraw Lipiodol®
using 20ml mixing s
- Withdraw anticance
syringe, using 20ml

of an emulsion
® Ultra Fluid
er agent drug.

now perform
elective cTACE

Recommended

- Anticancer agen
epirubicin[3], cisplatin[4], mitomycin[5]
- Ratio to follow: **1 drug volume to 2 Lipiodol® Ultra Fluid volumes**

IMPORTANT!

Caution

- **A maximum of 15ml Lipiodol® Ultra Fluid** can be administered to the patient
- Always maintain the **appropriate ratio** between anti-cancer drug and Lipiodol® Ultra Fluid

Recommended

- The **quality of emulsion** should be assessed with a **"drop test"**[2]
> Water-in-oil and oil-in-water

Example:

A standard amount of **50mg of Doxorubicin powder** would be **re-suspended in 5ml** of sterile water/saline solution. For a **1:2 ratio** we would therefore **use 10ml of Lipiodol® Ultra Fluid,** obtaining a **total volume of 15ml.**

With courtesy of Pr. Thierry De Baere.

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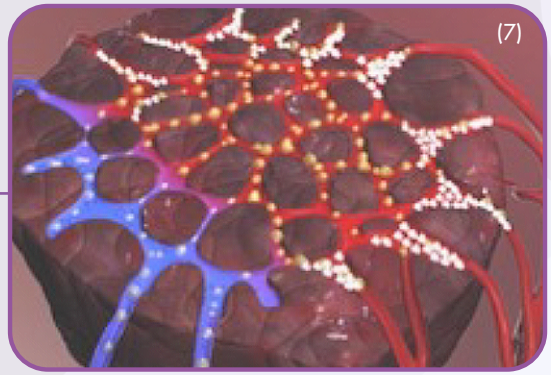
PROCEDURE

KEY GOLDEN RULES FOR AN OPTIMAL STANDARDIZATION PROCEDURE IN cTACE: MIXTURE PREPARATION & ADMINISTRATION OF EMBOLIC MATERIAL

II. ADMINISTRATION OF EMBOLIC MATERIAL

*«**Complete** the cTACE procedure by injecting embolic material: Gelatin Foam or Embolic particles. Additional feeder embolization should be systematically performed after emulsion injection. Hand-cut gelatine sponge is favored[2].»*

Gelatin-Foam: widely used embolic materials



- **Embolization of the tumor** through its vessel
  > The particles cannot penetrate the tumor **therefore allowing blockage of arterial entries.**
- **Complete recanalization** in 1-2 weeks
  > Allows for **subsequent cTACE treatment** through the same tumor feeders.
- ***«Gelatine sponge particles** are the most commonly used embolic material and are associated with arterial recanalization within 1–2 weeks after embolization. This allows for subsequent TACE retreatment through the same tumor feeders[2].»*

- **Key take aways:**
  > cTACE, standardization consists in preparing the anticancer agent in a water-in-oil emulsion before administration[1]. It has been widely demonstrated that a water-in-oil emulsion made of droplets (i.e., an Internal phase containing drug in aqueous solution and a continuous external phase of oily Lipiodol) is more densely retained within the tumors than the alternative oil-in-water emulsion[2].
- **Key golden rules for an optimal standardization procedure in cTACE[1]:**
  > Importance of the ratio between Lipiodol® Ultra Fluid and anticancer agent during the mixture preparation :1 drug volume to 2 Lipiodol® Ultra Fluid volumes.
  > Anti-cancer drug should be first pushed towards the syringe containing Lipiodol® Ultra-Fluid: water-in-oil emulsion[6].
  > Complete the cTACE procedure by injecting embolic material: Gelatin Foam or Embolic particles.
- **Materials to perform the procedure:**
  > Lipiodol® Ultra Fluid, 480 mg Iodine/mL, solution for injection.
  > Vectorio®: Lipiodol® Ultra Fluid Resistant Mixing and Injection System for Conventional Trans-Arterial Chemoembolization.

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