

# When Medications Mix with Contrast Agents: The Intersection of Pharmacy and Radiology for Patient Safety and Compliance

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**Presented as a Live Webinar**

Tuesday, April 25, 2017  
1:00 PM – 2:00 PM ET

## **On-demand Activity**

Live webinar recorded and archived to be watched at your convenience  
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[www.ashpadvantage.com/go/contrastagents](http://www.ashpadvantage.com/go/contrastagents)

Planned by ASHP Advantage and supported by an educational grant from Guerbet Group



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## Activity Overview

This educational activity will describe how hospital pharmacists can become involved in the oversight and use of contrast media in their institutions with a special emphasis on chemoembolization. Faculty will address the rationale and therapeutics of chemoembolization and provide examples of pharmacy and radiology collaboration. In addition, the role of the pharmacist in improving patient safety and the medication use process in the radiology suite will also be discussed.

## Learning Objectives

At the conclusion of this application-based educational activity, participants should be able to

- Describe the methods of transarterial chemoembolization (TACE).
- List five practical considerations for traditional TACE of which pharmacists should be aware.
- Outline a process for pharmacy-radiology collaboration in the medication use process and patient safety procedures.
- Discuss opportunities for pharmacists to improve patient safety during diagnostic procedures.
- Describe The Joint Commission standards relating to medication management in radiology.

## Continuing Education Accreditation



The American Society of Health-System Pharmacists is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

This activity provides 1.0 hour (0.1 CEU – no partial credit) of continuing pharmacy education credit.

Live Activity ACPE #: 0204-0000-17-433-L05-P

On-demand Activity ACPE #: 0204-0000-17-433-H05-P

**Qualifies for  
Patient Safety CE**

Participants will process CPE credit online at <http://elearning.ashp.org/my-activities>. CPE credit will be reported directly to CPE Monitor. Per ACPE, CPE credit must be claimed no later than 60 days from the date of the live activity or completion of a home-study activity.

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## Faculty

### **Eugene R. Przespolewski, Pharm.D., BCOP**

Senior Oncology Pharmacist  
The Jonah Center for Oncology and Hematology  
Erie County Medical Center  
Buffalo, New York

Eugene R. Przespolewski, Pharm.D., BCOP, is Senior Oncology Pharmacist at Erie County Medical Center (ECMC) in Buffalo, New York. In addition, Dr. Przespolewski is a faculty member at the University at Buffalo and also serves as a preceptor to pharmacy students from D'Youville College of Pharmacy and the University at Pittsburgh School of Pharmacy. He also precepts PGY-1 pharmacy residents in hematology/oncology from the University at Buffalo School of Pharmacy.

Dr. Przespolewski joined Erie County Medical Center in 2011 and assumed responsibility for starting a hematology/oncology pharmacy practice. He also facilitated clinical pharmacy involvement in the practice through Collaborative Drug Therapy Monitoring in chemotherapy-induced nausea and vomiting, oral chemotherapy monitoring program, and others.

Dr. Przespolewski graduated from Canisius College with a Bachelor of Science in Biochemistry and a minor in Classical Studies. He received his Doctor of Pharmacy degree from the University at Buffalo School of Pharmacy and Pharmaceutical Sciences.

Dr. Przespolewski has several publications and research projects in the fields of hematology and oncology. His research interest includes optimization of supportive care in oncology patients and health systems optimization of pharmacy internship program.

## **When Medications Mix with Contrast Agents: The Intersection of Pharmacy and Radiology for Patient Safety and Compliance**

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### **Sameer Gadani, M.D.**

Assistant Professor of Interventional Oncology  
Department of Interventional Radiology  
St. Louis University Hospital  
St. Louis, Missouri

Sameer Gadani, M.D., is Assistant Professor of Interventional Radiology at Saint Louis University and provides services at Saint Louis University Hospital and St. Mary's Hospital. He trained at the University of Minnesota Medical Center and University of Texas MD Anderson Cancer Center for Interventional Radiology and Interventional Oncology. He has been working at Saint Louis University for the last four years. Before that he served as a faculty for four years at LSU-New Orleans and University of Minnesota Medical Center.

Dr. Gadani specializes in Interventional Oncology with focus on Locoregional therapy for liver cancer. His clinical and research interests include trans-arterial chemoembolization, radioembolization and ablation of liver tumors. Additionally, he specializes in interventional procedures for kidney, lung, and MSK cancers. He has extensive experience in liver transplant-related interventions, complex portal hypertension management, UFE, varicose vein ablation, kyphoplasty/vertebroplasty and prostate artery embolization.

He has presented multiple abstracts at international conferences and authored several peer-reviewed publications related to Interventional Oncology. He is actively involved in training radiology residents, interventional radiology fellows, and medical students.

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## When Medications Mix with Contrast Agents

The Intersection of Pharmacy and Radiology for Patient Safety and Compliance



**Eugene R. Przespolewski, Pharm.D., BCOP**  
Senior Oncology Pharmacist  
The Jonah Center for Oncology and Hematology  
Erie County Medical Center  
Buffalo, New York

**Sameer Gadani, M.D.**  
Assistant Professor of Interventional Oncology  
Department of Interventional Radiology  
St. Louis University Hospital  
St. Louis, Missouri

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1.0 hr CE

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- Describe the methods of transarterial chemoembolization (TACE).
- List five practical considerations for traditional TACE of which pharmacists should be aware.
- Outline a process for pharmacy-radiology collaboration in the medication use process and patient safety procedures.
- Discuss opportunities for pharmacists to improve patient safety during diagnostic procedures.
- Describe The Joint Commission standards relating to medication management in radiology.

## Transarterial Chemoembolization: What a Pharmacist Needs to Know

**Sameer Gadani, M.D.**  
Assistant Professor  
Division of Interventional Radiology  
Saint Louis University Hospital  
St. Louis, Missouri

**Which type of transarterial chemoembolization (TACE) is performed more frequently at your institute?**

- Conventional TACE
- Drug-eluting beads TACE
- Both

**What are the indications of transarterial chemoembolization?**

- Hepatocellular carcinoma (HCC)
- Colorectal metastasis to liver
- Neuroendocrine metastasis to liver
- All of the above

### Transarterial chemoembolization is



- a. Curative treatment
- b. Palliative treatment
- c. Both

### Conventional TACE involves hepatic artery injection of



- a. Chemotherapeutic agents
- b. Chemotherapeutic agents + ethiodized oil (Lipiodol®)
- c. Chemotherapeutic agents + ethiodized oil followed by embolization

### Which of the following chemotherapeutic agents cannot be 'loaded' on the beads?



- a. Doxorubicin
- b. Irinotecan
- c. Mitomycin C
- d. Cisplatin

### Indications

- Hepatocellular carcinoma
- Metastatic colorectal tumor
- Neuroendocrine tumor metastasis to liver
- Cholangiocarcinoma
- Breast cancer/sarcoma??

### Hepatocellular Carcinoma

- Hepatocellular carcinoma (HCC) is a primary liver tumor and commonly seen in patients with cirrhosis secondary to variety of causes, including Hepatitis C, Hepatitis B, alcohol, and non-alcoholic fatty liver.
- Most common liver malignancy and one of the leading cause of cancer-related deaths worldwide.
- Surveillance of high-risk population helps in identification of HCC at an early stage when potentially curative therapies such as surgical resection or liver transplant can be offered with 5 year survival up to 75%.

Mauer K et al. *Curr Gastroenterol Rep.* 2015; 5:442.

### Hepatocellular Carcinoma (cont.)

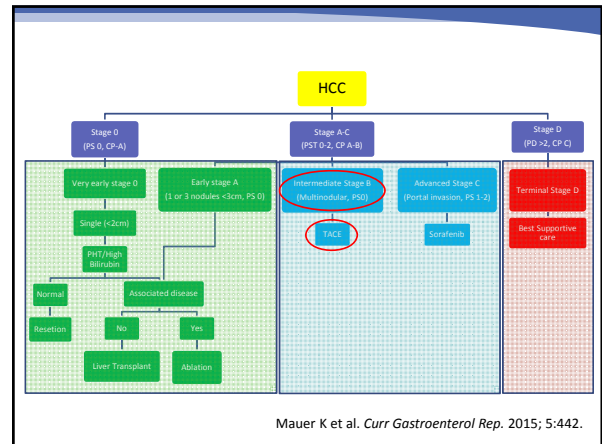
- However, more than 50% of patients with HCC are diagnosed at a stage when curative therapies cannot be offered.
- In these patients palliative therapies such as transarterial chemoembolization or transarterial radioembolization are offered.

Mauer K et al. *Curr Gastroenterol Rep.* 2015; 5:442.

## Hepatocellular Carcinoma (cont.)

- Therapies offered to the patient with advanced HCC depends on number and size of tumor(s), liver function, performance status, vascular invasion, and presence of extrahepatic disease.
- Barcelona clinic liver cancer (BCLC) classification is the most accepted system for stratification and recommendation of treatment for HCC.

Mauer K et al. *Curr Gastroenterol Rep.* 2015; 5:442.



Mauer K et al. *Curr Gastroenterol Rep.* 2015; 5:442.

## Colorectal Cancer Metastasis

- Colorectal cancer is third most common cancer worldwide
- Synchronous metastasis in the liver is present in 15-20% patients and metachronous in more than 50% patients
- Liver is most common site of metastasis. It is only site of metastasis in 40% patients.
- Surgical resection of the primary site, resection of the liver metastasis (possible in only 20% patients) and chemotherapy is standard of care.

Richardson AJ et al. *J Vasc Interv Radiol.* 2013; 25:1209-17.

## Colorectal Cancer Metastasis (cont.)

- For the patients with surgically unresectable metastasis
  - 5 FU and leucovorin (median survival 12 months)
  - Irinotecan and oxaliplatin (median survival 20 months)
  - Bevacizumab or cetuximab (additional benefit)
- TACE is offered to patients with nonresectable liver metastasis. It is offered concomitant with chemotherapy or patients who responded poorly or are refractory to chemotherapy.

Richardson AJ et al. *J Vasc Interv Radiol.* 2013; 25:1209-17.

## Neuroendocrine Tumors Metastatic to Liver

- Neuroendocrine tumors originate from foregut, midgut, or hindgut.
- Presence of liver metastasis negatively impacts prognosis.
- Treatment options include surgical resection, TAE, TACE, or radioembolization.

TAE = Transarterial embolization

Kennedy AS et al. *HPB.* 2015; 17:29-37.

## Rationale for TACE

- Liver has dual blood supply via hepatic artery and portal vein.
- 70% of blood supply to the liver is through the portal vein, and 30% is from hepatic artery.
- Dominant blood supply to the liver tumor is through the hepatic artery (80%) and portal vein branches (20%).
- Intra-arterial injection of chemotherapeutic agents along with embolic material ensures their high concentration in the tumor with minimal effect on the normal liver.



## Types of TACE

- Conventional TACE (cTACE)
- Drug-eluting beads TACE (DEBTACE)

## Conventional TACE

- Components
  - Chemotherapeutic agents (doxorubicin, mitomycin C)
  - Ethiodized oil
  - Embolic material
    - Sterile compressed sponge (Gelfoam®)
    - Polyvinyl alcohol (PVA) embolization particles (Contour™)
    - TAG microspheres (MagPlex®)

## Conventional TACE (cont.)

- Rationale
  - Single drug therapy – doxorubicin
  - Combination drug therapy – doxorubicin, mitomycin C
  - Embolization combined with the delivery of drugs with high hepatic extraction ratios and steep dose-response curve can maximize the advantage of local delivery.
  - Complete embolization results in zero extraction of these agents by the liver.
  - Pharmacokinetics of these chemotherapeutic agents are altered when combined with ethiodized oil.

Zamboni CG et al. *Interventional Oncology* 360. 2015; 3:E121-E136.

## Conventional TACE (cont.)

- The emulsion allows prolonged transit of the drugs within the tumor bed, allowing greater contact time between the cancer cells and chemotherapeutic agents.
- Embolization with Gelfoam® or microparticles after the injection of the emulsion further increases contact time.
- This leads to higher tumor and systemic drug concentration ratio.

Dubbelboer IR et al. *Ther Deliv*. 2014; 5:447-66.

## Conventional TACE (cont.)

- Ethiodized oil (Lipiodol®)
  - Iodinated and ethylated poppy seed oil.
  - Key component because it can carry chemotherapy agents, tumor seeking, and embolic effect.
  - After injection into the hepatic artery it is preferentially accumulated in the tumor tissue for three months as extracellular lipid layers (nonglobular) or as intracellular droplets (globular).

Liapi E et al. *Cardiovas Intervent Radiol*. 2011; 34:37-49.

## Conventional TACE (cont.)

- Higher density – keeps the emulsion stable.
- Higher than blood viscosity – embolic effect.
- It is distributed through the hepatic arterioles in the peribiliary plexus reaching up to its portal venules (dual embolic effect).

Vazquez BY et al. *Vasc Health Risk Manag*. 2012; 8:1-6.

### Conventional TACE (cont.)

- Formation of emulsion, basic pharmacokinetics, and mechanism of action
  - Single agent: doxorubicin 50 mg diluted in water, soluble contrast for 10 mL volume.
  - Combination: cisplatin 100 mg, doxorubicin 50 mg and mitomycin C 10 mg diluted in water soluble contrast for 10 mL volume. Consult your protocol for specific admixture directions.
  - Polycarbonate or glass syringes/three way stopcocks.

### Conventional TACE (cont.)

- 10 mL aqueous solution (chemo) and 15-20 mL ethiodized oil.
- Vigorous mixing (30-40 times) to prepare **WATER IN OIL** emulsion.
- Release of doxorubicin from the lipiodol depends on
  - Ratio of aqueous and lipid phase.
  - Stability of emulsion.
  - Type of mixing procedure (vigorous mixing – with goal of inner and outer droplet size of 20 and 100 microns, respectively).

Dubbelboer IR et al. *Ther Deliv.* 2014; 5:447-66.

### Conventional TACE (cont.)

- Doxorubicin use in HCC is an off-label use. Once released, doxorubicin damages the DNA of the tumor cell by
  - Binding to topoisomerase II
  - Intercalation to DNA base pair
  - Free radical formation

Tacar O et al. *J Pharm Pharmacol.* 2013; 65:157-70.

### Transarterial chemoembolization with drug-eluting beads (DEB-TACE)

- DEB-TACE is most frequently used TACE technique in western world.
- DEB-DOX for HCC (doxorubicin) and irinotecan eluting beads (DEBIRI) for mCRC (irinotecan)
- Microspheres (e.g., QuadraSpheres®) can be loaded with cisplatin

Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.

### Transarterial chemoembolization with drug-eluting beads (DEB-TACE)

- Rationale
  - Beads can be eluted with chemotherapeutic agents
  - They can carry the chemo agents up to the tumor and release them over the period of hours
  - Beads also have embolic effect leading to tumor hypoxia and infarction
  - Ratio of concentration of chemotherapy agents in the tumor: plasma markedly high
  - Improved pharmacokinetics over conventional TACE
  - Relatively less pain

Varela M et al. *J. Hepatol.* 2007; 46:474-81.

### Transarterial chemoembolization with drug-eluting beads (DEB-TACE)

- Beads
  - DC beads – doxorubicin or irinotecan
    - 75-100 microns up to 500-700 microns
  - LC beads LUMI™
  - SAP-MS (superabsorbent polymer microspheres) – QuadraSpheres®
  - Precision beads – preloaded with doxorubicin (37.5 mg/mL)
  - Paragon beads – preloaded with irinotecan

### How to load, mechanism of action, and pharmacokinetics

- DC Beads
  - Approved for hypervascular tumor. Off label use for drug sequestration and TACE.
  - DC beads sequester oppositely charged drugs through ion exchange mechanism.
  - Maximum loading – 45 mg/mL (doxorubicin) and 50-60 mg/mL (irinotecan)
  - Ideal loading – 37.5 mg/mL (doxorubicin).
  - Drug sequestration depends on bead size, concentration of drug, and salt-loading solution concentration.

Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.

### How to load, mechanism of action, and pharmacokinetics (cont.)

- Bead size decreases after sequestration. Larger beads decrease in size more than the smaller beads.
- SAP-MS – biocompatible, hydrophilic, and nonresorbable
  - SAP-MS increase in size four times after sequestration.
  - They can absorb fluid 64 times their dry volume.
  - Doxorubicin or cisplatin can be loaded.
  - FDA approved for TACE.

Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.

### How to load, mechanism of action, and pharmacokinetics (cont.)

- Drug eluting beads are injected into the arteries reaching up to the tumor.
- Beads cause embolization of the arteries and also slowly release doxorubicin in exchange for cations.
- Release of doxorubicin from the beads depends on bead size and concentration of doxorubicin. Released up to 30 days.
- Highest concentration of doxorubicin in the tissue noted adjacent to the beads. Quantifiable plasma concentration seen up to 7 days.

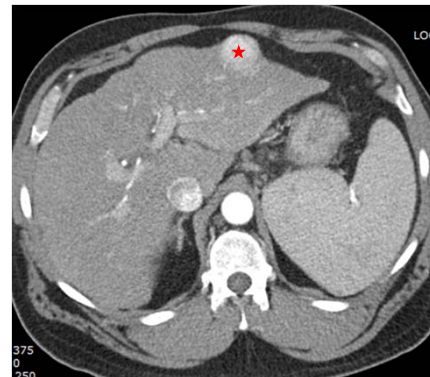
Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.

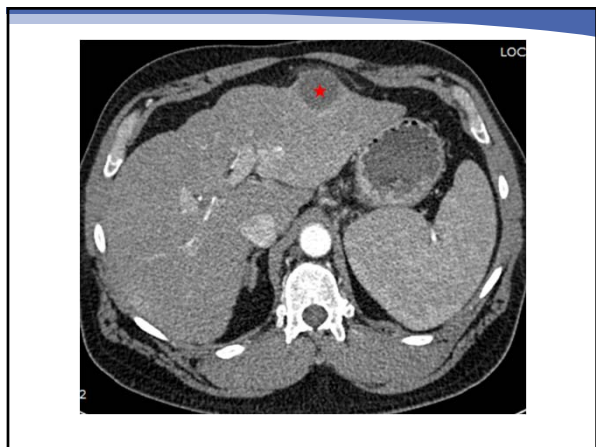
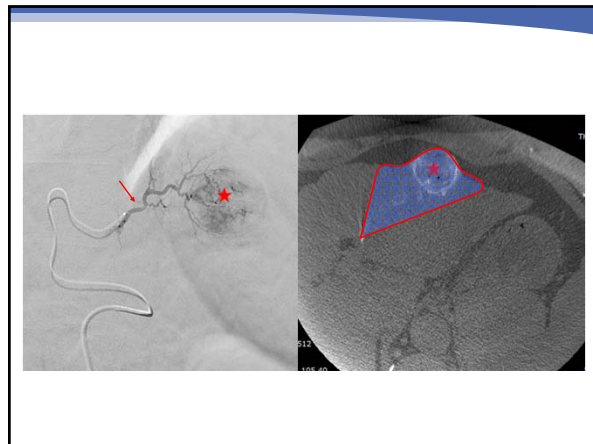
### Pre-procedure Assessment

- Clinic visit
- Confirming eligibility for TACE
- Labs
  - CBC
  - CMP
  - Coagulation studies (e.g. aPTT, PT, d-dimer, fibrinogen)
  - AFP
  - Model for end-stage liver disease (MELD), Child-Pugh score
  - Liver function tests
- Eastern Cooperative Oncology Group (ECOG) performance status.
- MRI/CT scan of the liver (three phases)

### Pre-procedure Assessment

- Day of the procedure
  - Cefazolin 1 gm i.v. (optional)
  - Dexamethasone 10 mg i.v.
  - Ondansetron 8 mg i.v.
  - Diphenhydramine 50 mg i.v.
  - 0.9% sodium chloride injection 75 mL/hr for 6-8 hrs (pre-intra-post procedure)
- Post procedure
  - Narcotics (prn)
- Clinic visit in 6 weeks with imaging





### Key Takeaways

- Key take away #1: TACE is offered as palliative treatment for primary hepatocellular carcinomas and few other primary tumors metastasized to the liver.
- Key take away #2: Ethiodized oil (Lipiodol®) is an excellent carrier of chemotherapy agents and is a key ingredient of conventional TACE. "Water in oil" is ideal emulsion for intra-arterial injection.
- Key take away #3: Different sizes and types of drug-eluting beads are available, which can carry doxorubicin, irinotecan, or cisplatin.

## The Harmony of Radiology and Pharmacy: TACE and Chemoembolization

Eugene R. Przespolewski, Pharm.D., BCOP  
Senior Oncology Pharmacist  
Erie County Medical Center  
Buffalo, New York

**Contrast agents are considered medications according to the Joint Commission?**

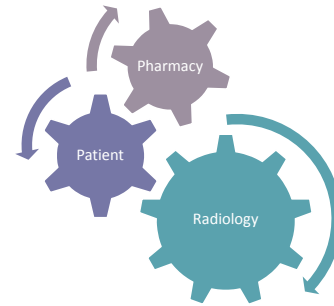
a. True  
b. False

## TACE in a Nutshell

- TACE is a form of liver-directed or local therapy (as opposed to systemic)
- Ethiodized oil (Lipiodol®) and drug-eluting beads (“DEBs”) serve multiple purposes
  - Delivery of directed cytotoxicity
  - Control and prolong effect in tumor microenvironment
  - Act as or contain contrast
- The goal is to maximize kill and minimize toxicity
- Harmony of radiology and pharmacy

TACE = Transarterial chemoembolization therapy

## The Machinery in Motion



## The Marriage of Radiology and Pharmacy

- The Joint Commission: contrast media are medications
- Contrast media are subjected to same scrutiny as other medications
  - Storage requirements
  - Review of orders
  - Medication labeling
  - Medication dispensing
- Should be recorded in electronic medical record (EMR) and orderable via computerized physician order entry (CPOE)

The Joint Commission. *Joint Commission Perspectives*. 2005; (25)6:9.  
Norenberg JP. *Pharmacy Purchasing & Products*. 2011; 8(4):2.

## Case of Contrast Contamination

- Patients in Arizona pain clinic injected with diluted contrast agent to guide epidural injections
  - Single dose of contrast agent
- Personnel diluted contrast agent and placed in a separate vial to be used as a multidose vial (MDV)
  - MDV contaminated with methicillin-resistant *Staphylococcus aureus* (MRSA)
- 3 patients developed severe infections

Centers for Disease Control and Prevention. Invasive *staphylococcus aureus* infections associated with pain injections and reuse of single-dose vials – Arizona and Delaware, 2012. *Morb Mortal Wkly Rep (MMWR)*. 2012; 61 (27); 501-504.

## ISMP Recommendations

- Confusion over pharmacy bulk pack (PBP) container vs. MDV
  - PBPs contains multiple single doses
  - PBPs do NOT contain preservatives
  - Special handling requirements labeled on packaging
- PBPs of contrast media to be drawn up in laminar airflow hoods
- Pharmacy department should develop rapport with radiology department

ISMP. *Medication Safety Alert*. (September 20, 2012).  
<http://www.ismp.org/Newsletters/acutecare/showarticle.aspx?id=31>  
(accessed 2017 Apr 25).

## Which of the following chemotherapeutic agents have been used in TACE procedures?

- a. DOXOrubicin
- b. Irinotecan
- c. MitoMYcin
- d. All of the above

## TACE Compounding & Preparation

- Institutions may already have established procedures
- Common chemotherapy used
  - DOXOrubicin
  - MitoMYcin
  - CISplatin
  - Irinotecan
- cTACE and DEB-TACE have distinct compounding processes
  - DEB manufacturers have different load times
  - Choice in bead size must be specified

Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.

## DOXOrubicin in TACE

- MOA: Anthracycline antibiotic
  - Major: DNA-intercalation stabilizing Topoisomerase II
- Dose: No standard dosing
  - Flat dosing: 50 – 150 mg
  - BSA dosing: 50 – 75 mg/m<sup>2</sup>
- PK/PD: based on TACE procedure
  - Ethiodized oil (Lipiodol®): Technique dependent, variable C<sub>max</sub>, larger AUC
  - DEB: Bead size dependent, consistent release

Tam K. The roles of doxorubicin in hepatocellular carcinoma. *ADMET & DMPK.* 2013; 3: 29-44. Abstract.  
Varela M et al. *J Hepatol.* 2007; 46:474-81.

## Conventional TACE Compounding

- Chemotherapy + ethiodized oil + embolizing agents
- Drugs mixed with ethiodized oil to form an emulsion
  - Water-in-oil emulsion is preferred
- Volume of drug must be minimized
  - Preference for DOXOrubicin powder drug source
- Drug mixed with ethiodized oil in interventional radiology (IR) suite
  - Drug pushed into ethiodized oil

de Baere T et al. *Cardiovasc Intervent Radiol.* 2016; 39:334-43.

## Drug-Eluting Beads Compounding

- Product specific compounding processes
  - LC Beads®
  - QuadraSphere® (HepaSphere in Europe)
- Not FDA approved for use in USA
- Can use DOXOrubicin solution products
- Beads need to be “loaded,” with drug prior to use
  - Requires time to dwell
  - More complex compounding procedure

Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.

**According to USP Chapter <800>, which of the following is considered a risk of exposure to an HD?**

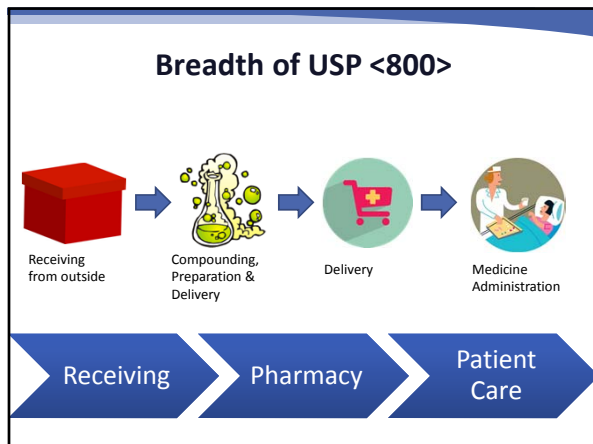


- a. Loading the DEB-TACE with doxorubicin
- b. Delivering the DEB-TACE to the IR suite
- c. Administering DEB-TACE to the patient in the IR suite
- d. Two of the above
- e. All of the above

## TACE and USP Chapter <800>

- USP Chapter <800>: practice and quality standards for handling hazardous drugs (HDs)
  - Protects healthcare worker, patient and everyone between
- USP Chapter <800> builds on USP Chapters <795> and <797>
- No exposure to HDs is acceptable
  - Protect yourself and others
- TACE brings HDs to nontraditional areas

USP <800> Hazardous Drugs 2016.



### Compounding TACE and USP Chapter <800>

- Know your institutions HD list
  - May be less/more stringent than NIOSH list
- Compounding TACE should be done in a biological safety cabinet (BSC) inside a negative pressure room
- Some DEBs require time to load
  - USP Chapter <797> compliance: BUD requirements
  - May not be feasible in some infusion clinics
- All agents manipulated in BSC are considered HD due to environmental exposure

BUD : Beyond-use date USP <800> Hazardous Drugs 2016.

### CSTD and Administration of Drugs

- NIOSH first to endorse/define the idea in 2004
- CSTD Examples
  - BD PhaSeal®
  - BBraun OnGuard®
- Compounding: CSTD *should* be used
- Administration: CSTD *must* be used
  - Caveat: when dosage form allows
- Discussion as to best approach this with TACE

NIOSH. Hazardous Drugs in Health Care Settings 2004.  
USP <800> Hazardous Drugs 2016.

CSTD: Closed-system transfer device

### USP Chapter <800> Educational Expectations

- Establishment of SOP, reviewed annually
- Annual HD handling competencies specific to job function
  - Overview of the entity's list of HD and their risks
  - Review the entity's SOPs related to handling HD
  - Proper use of personal protective equipment (PPE)
  - Proper use of equipment and devices (CSTDs)
  - Response to known/suspected HD exposure
  - Spill management
  - Proper disposal of HDs and trace-contaminated materials

USP <800> Hazardous Drugs 2016.

### Other USP Chapter <800> Considerations

- Transport issues
  - Minimize risk of breakage and leakage
  - Do NOT use the pneumatic tube system
- Users must have appropriate PPE
- Must be labeled clearly as a HD
- Stored in spill-proof area
- Must have spill kit readily available
- Must know how to dispose hazardous waste
  - Anything exposed to drugs considered HD

USP <800> Hazardous Drugs 2016.

### Summary of Compounding Pearls

- Collaboration/communication with radiology department
- Understanding USP Chapter <800> practical concerns
- Trained in procedures for institutional preferences
  - DEB-TACE vs. cTACE
  - Protocol?
  - How much advance notice
    - Appropriate lead time to order products

**Do you have a pharmacy protocol in place to promptly manage a TACE order?**



- a. Yes
- b. No
- c. Maybe
- d. I don't know

## Data for Therapy

- Hepatocellular carcinoma
  - Unresectable
  - Adjunct therapy to liver resection
  - Bridge to liver transplant
  - Combination with radiofrequency ablations
- Unresectable cholangiocarcinoma
- Neuroendocrine tumor metastased to the liver
- Metastases to the liver with the following primary malignancies
  - Breast
  - Sarcoma
  - Colorectal

Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.

## Pre-operative Considerations

- Patients should fast for at least 4 – 6 hours
- Hydration
- Antiemetics: Consider DOXOrubicin
  - NCCN moderate emetogenicity
    - Dexamethasone 20 mg on day 1, 8 mg days 2 & 3
    - Granisetron 3 mg on day 1
- Antibiotics: controversial
  - May not be necessary
  - Higher risk: biliary tract disease/reconstruction
- Analgesics

NCCN: National  
Comprehensive Cancer  
Network

de Baere T et al. *Cardiovasc Intervent Radiol.* 2016; 39:334-43.  
Ogasawara S et al. *J Clin Oncol.* 2016; 34 suppl; abstr 4071.  
Wang J et al. *Can J Gastroenterol.* 2012; 26:85-91.

**Which of the following is NOT a symptom of postembolization syndrome?**



- a. Nausea and vomiting
- b. Liver abscesses
- c. Abdominal pain
- d. Fever

## Post-operative Complications

- Majority of patients receive 1 – 2 doses
- Most common complication
  - Transient transaminitis
  - Postembolization syndrome
- Major post-operative complications are rare
  - Liver infarction
  - Cholecystitis
  - Intrahepatic abscesses
  - Pancreatitis

Liapi EA et al. *Cardiovasc Intervent Radiol.* 2011; 34:37-49.  
de Baere T et al. *Cardiovasc Intervent Radiol.* 2016; 39:334-43.

## Postembolization Syndrome (PES)

- Sequela of cytotoxicity and inflammation
  - Nausea
  - Vomiting
  - Abdominal pain
  - Fever
- DEB-TACE may have lower rate
- May be associated with worsened prolonged survival

Mason MC et al. *HPB.* 2015 Dec; 17(12): 1137 – 1144.



## PES Management

- Transaminitis: self-limiting ~ 7 days
- Analgesia
  - Intra-articular lidocaine with procedure: cTACE
  - Opiates: Pre- and post-procedure
- Antiemetics
  - 5-HT3 Antagonists: scheduled
  - Dexamethasone
- Antibiotics: Not warranted
  - Fever is not infection

Blackburn H, et al. *Cancer Nursing*. 2016 (39)5: E1- 18.

## Key Takeaways

- Key Takeaway #1
  - Develop a working relationship with Radiology Department to facilitate patients undergoing TACE
- Key Takeaway #2
  - Compounding procedures are institution-specific and USP Chapter <800> poses unique barriers to overcome
- Key Takeaway #3
  - There are unique pre- and post-operative issues in patients undergoing TACE

**Which of these practice changes will you consider making? (Select all that apply.)**



- a. Foster/build relationship with radiologists to better care for TACE patients
- b. Evaluate current TACE protocol or develop one
- c. Review/change chemotherapy prep procedure
- d. Optimize protective measures of USP Chapter <800> in TACE preparation
- e. Utilize complication management strategies to decrease LOS and increase patient satisfaction

## Selected Resources

- de Baere T, Arai Y, Lencioni R et al. Treatment of liver tumors with Lipiodol TACE: Technical Recommendations from Experts Opinion. *Cardiovasc Intervent Radiol*. 2016; 39:334-43.
- Liapi E, Geschwind JF. Transcatheter arterial chemoembolization for liver cancer: is it time to distinguish conventional from drug-eluting chemoembolization? *Cardiovasc Intervent Radiol*. 2011; 34:37-49.
- USP Chapter <800> Hazardous Drugs-Handling in Healthcare Settings.

# When Medications Mix with Contrast Agents: The Intersection of Pharmacy and Radiology for Patient Safety and Compliance

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## Assessment Test



This assessment test has been provided as a study aid only. Follow the prompts at the end of the presentation to claim credit. Credit must be claimed within 60 days of completing the activity.

1. Transarterial chemoembolization (TACE) is offered in which Barcelona clinic liver cancer (BCLC) stage of hepatocellular carcinoma (HCC)?
  - a. Very early stage.
  - b. Early stage.
  - c. Intermediate stage.
  - d. Advance stage.
  - e. Terminal stage.
2. Which specific characteristics of the blood supply to the liver allows performance of TACE without affecting liver function?
  - a. Dual blood supply to the liver by portal vein and hepatic artery.
  - b. Tumor primarily supplied by portal vein.
  - c. Liver parenchyma primarily supplied by hepatic artery.
  - d. Liver blood supply is primarily through the hepatic artery.
3. Ideal emulsion for conventional TACE is
  - a. Water in oil.
  - b. Oil in water
4. Which of the following is a characteristic that ethiodized oil (Lipiodol®) and drug-eluting beads DO NOT share when used for TACE?
  - a. Alters the pharmacokinetics of chemotherapeutic agents.
  - b. Allows greater time of contact between tumor cells and chemotherapeutic agent.
  - c. Chemotherapeutic agents are released to the tumor over a period of hours.
  - d. Leads to higher ratio of tumor to system drug concentration.
5. The ideal 'loading dose' of doxorubicin on DC beads is
  - a. 30.5 mg/mL
  - b. 37.5 mg/mL
  - c. 40.0 mg/mL
  - d. 60.0 mg/mL

## When Medications Mix with Contrast Agents: The Intersection of Pharmacy and Radiology for Patient Safety and Compliance

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6. Which of the following would NOT be among the pre-procedure medications given on the day of the TACE procedure?
  - a. Cefazolin: 1 gm i.v. (optional)
  - b. Dexamethasone: 10 mg i.v.
  - c. Ondansetron: 8 mg i.v.
  - d. Dextrose 5% injection 75mL/hr
  
7. Which of the following is NOT a recommendation of ISMP regarding pharmacy bulk packaging (PBP) containers?
  - a. Expiration date should be included on the PBP packaging.
  - b. Multiple single doses may be drawn from a PBP.
  - c. PBPs do not contain preservatives.
  - d. Single doses from PBPs can be drawn at the patient's bedside.
  
8. Which of the following statements is FALSE regarding USP Chapter <800>?
  - a. USP Chapter <800> builds upon USP Chapters <795> and USP <797>.
  - b. Small exposures of HDs are considered safe.
  - c. USP Chapter <800> are quality standards to promote safe handling of hazardous drugs.
  - d. Requires compounding of HD to be done in a biological safety cabinet in a negative pressure room.
  
9. What most accurately describes the use of CSTDs according to USP Chapter <800>?
  - a. Compounding: CSTDs must be used.
  - b. Compounding: CSTDs are not used.
  - c. Administration: CSTDs should be used.
  - d. Administration: CSTDs must be used.
  
10. The most common side effect experienced in patients undergoing TACE is?
  - a. Sepsis.
  - b. Liver infarction.
  - c. Cholecystitis.
  - d. Postembolization Syndrome.