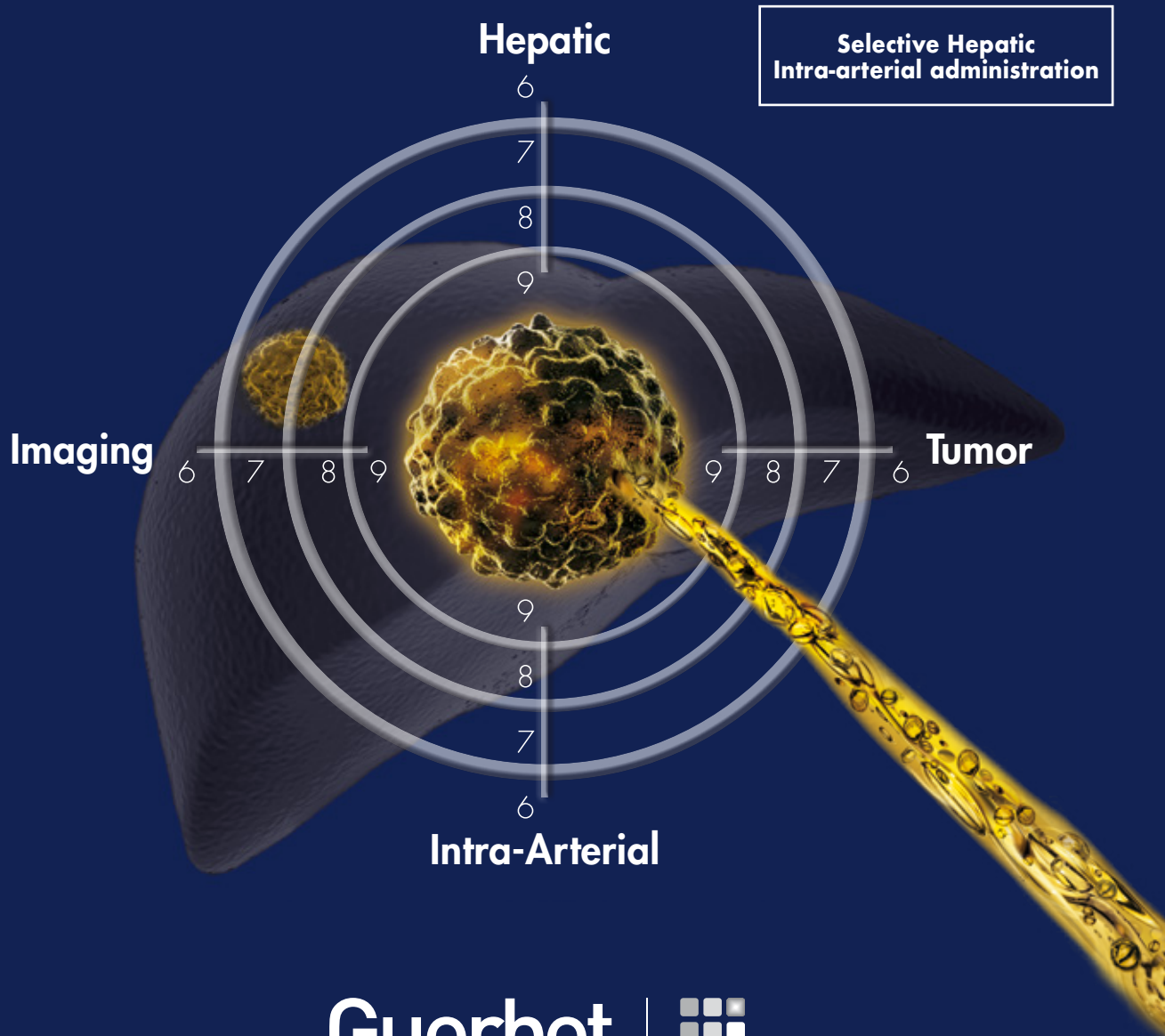


LIPIODOL[®]

(Ethiodized Oil) Injection

Imaging tumors in adults with known HCC



Guerbet | 

IMPORTANT SAFETY INFORMATION¹

WARNING: FOR INTRALYMPHATIC, INTRAUTERINE AND SELECTIVE HEPATIC INTRA-ARTERIAL USE ONLY.
See Full Prescribing Information for complete Boxed Warning.
Pulmonary and cerebral embolism can result from inadvertent intravascular injection or intravasation of Lipiodol. Inject Lipiodol slowly with radiologic monitoring; do not exceed recommended dose.

Important Safety information continued on back page



Contents

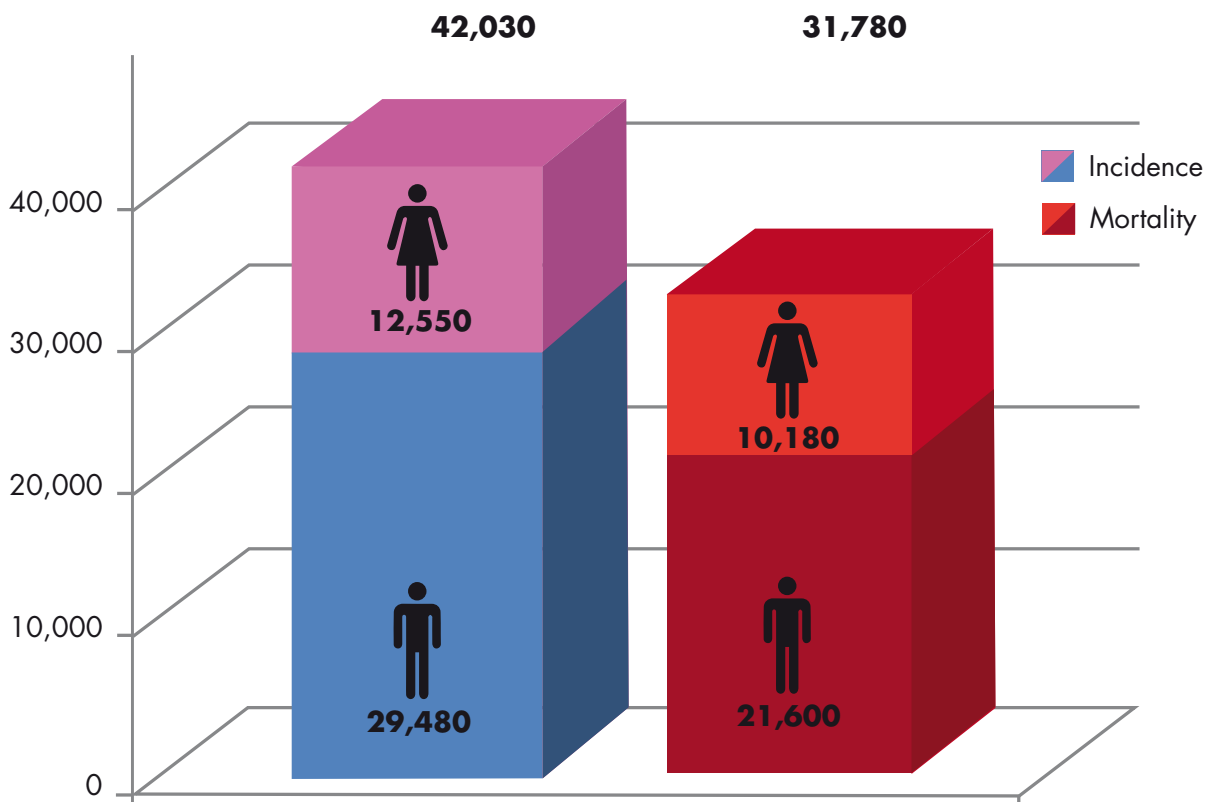
- 3** Primary Liver Cancer Epidemiology - US Snapshot
- 4** HCC Incidence - Global Snapshot
- 5** Lipiodol® Indication in HCC Patients
- 6** Lipiodol® in Liver CT
- 7** Efficacy - Ngan H. et al. Br. J. Radiol. (1990)
- 9** Efficacy - Jian-Jun Li. et al. World J Gastroenterol (2015)
- 10** Important Safety Information Continued



Primary Liver Cancer Epidemiology US Snapshot

The American Cancer Society's estimates for primary liver cancer and intrahepatic bile duct cancer in the United States for 2019 are:

- About 42,030 new cases (29,480 in men and 12,550 in women) will be diagnosed²
- About 31,780 people (21,600 men and 10,180 women) will die of these cancers²
- Liver cancer incidence has more than tripled since 1980. Liver cancer develops about 3 times more often in men than in women²
- Liver cancer death rates have increased to just over 2% per year since 2007²



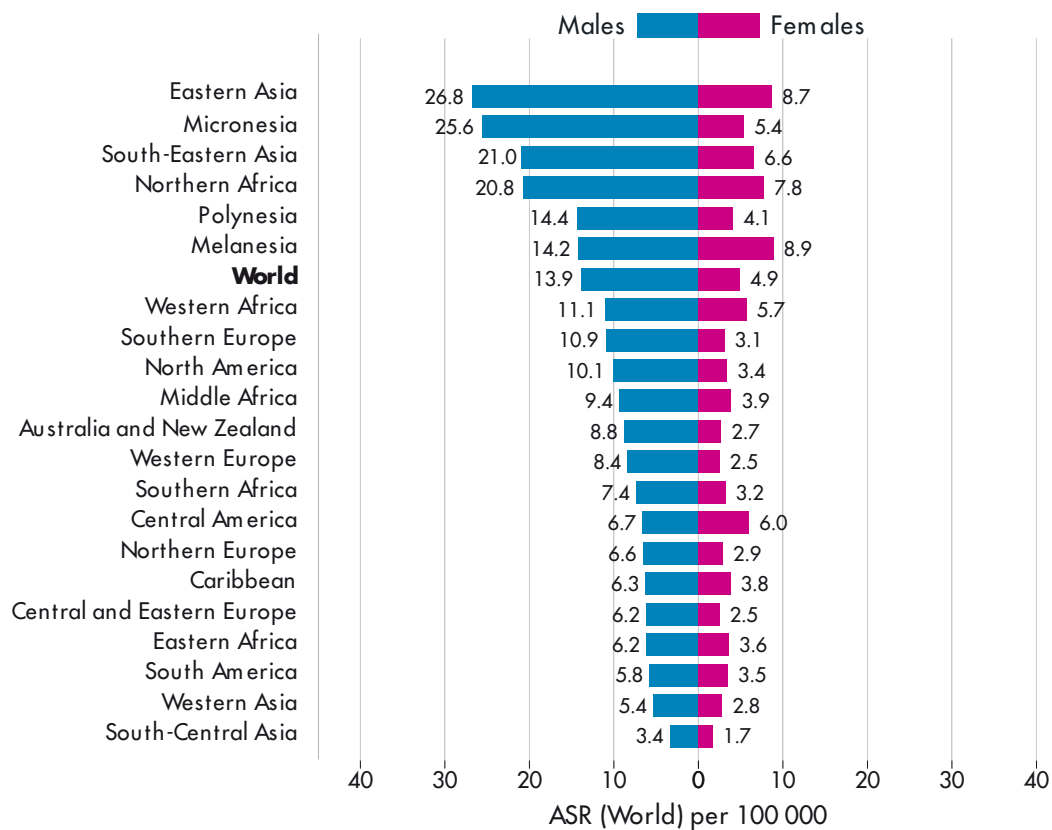


HCC Incidence - Global Snapshot

Worldwide Cancer Incidence and Mortality Statistics³

- More than 800,000 people are diagnosed with this cancer each year throughout the world³
- Liver cancer is also a leading cause of cancer deaths worldwide, accounting for more than 700,000 deaths each year³

Age standardized (World) incidence rates, liver, by sex³

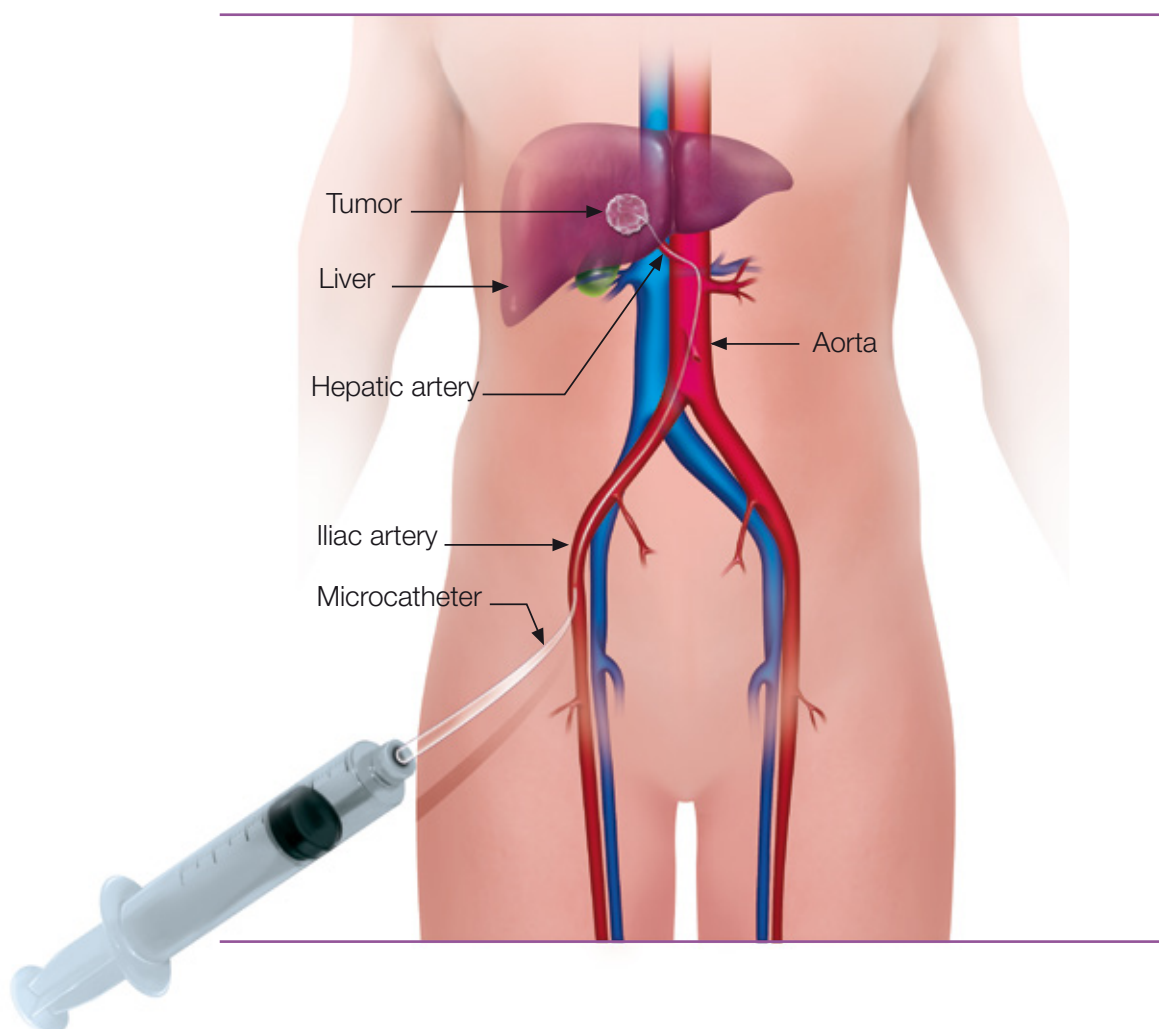


The Global Cancer Observatory - All Rights Reserved, March, 2019.



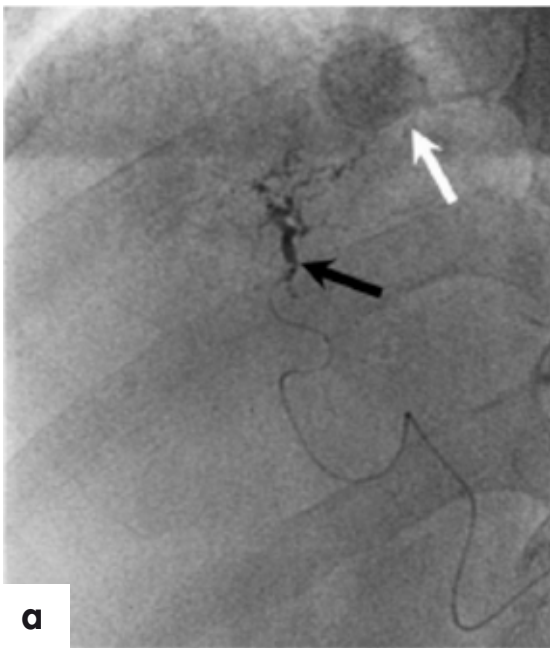
Lipiodol® (Ethiodized Oil) Injection Indication in HCC Patients

Lipiodol® is indicated for **selective hepatic intra-arterial** use for **imaging tumors** in adults with known **HCC**.



Lipiodol® (Ethiodized Oil) Injection in Liver CT

- Has a high affinity for primary hepatic tumors⁴
- Moves as oil droplets in the feeding vessels of hepatic tumors
- Deposits in the tumor when injected into the hepatic artery^{4,5}
- Retained in 85% of Hepatic tumors⁶
- Prolonged retention in liver tumors⁷



- (a)** A radiograph obtained during intra-arterial Lipiodol® injection. 2 mL of Lipiodol® was injected via the subsegmental branch of the right anterior hepatic artery (black arrow). Note the Lipiodol® retention in the subphrenic tumour (white arrow)⁸
- (b)** On 1-month follow-up CT showing a focal Lipiodol® accumulation (arrow)⁸



Efficacy

Ngan H. et al. Br. J. Radiol. (1990)⁸

AIMS

To evaluate the sensitivity & specificity of the techniques of Lipiodol[®] (ethiodized oil) injection – CT

Materials and Methods: Prospective, single center study

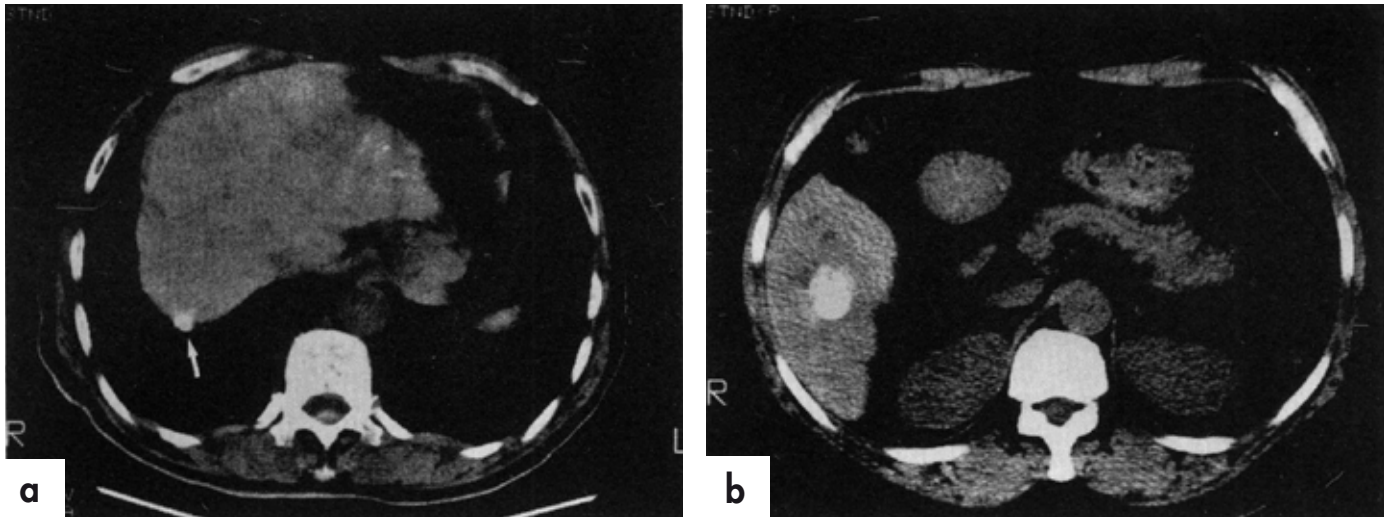
- **60 patients** suspected of having an HCC
- Lipiodol[®]-CT was performed 6-13 days following intra-arterial injection of Lipiodol[®]

Objectives

- To investigate the specificity of Lipiodol[®]-CT
- Evaluate whether Lipiodol[®] can detect an HCC while it is small and asymptomatic
- Evaluate whether if resectability rate can be improved
- To analyze the pattern of uptake of Lipiodol[®] by the tumor

Results

- The size of the HCCs ranged from 0.8 cm to 11 cm in diameter with the median size at 2.2 cm.
- Four uptake patterns were found: homogeneous, patchy, no uptake, faint uptake by the liver.
- ...In the diagnosis of HCC, Lipiodol[®]-CT had an overall **sensitivity of 97.1%**, an accuracy of 88.3% and a **specificity of 76.9%** [...].



(a) A 0.8 cm HCC with dense homogeneous uptake of Lipiodol® (arrow) in right lobe of the liver
(b) An HCC 2.5 x 1.8 cm with dense homogeneous uptake in the right lobe.

Conclusion

- ... for high risk patients, Lipiodol® (ethiodized oil) injection - CT is useful in the detection of HCCs while they are relatively small. In view of its ability to demonstrate daughter nodules at times not seen by conventional CT or hepatic angiography, the technique helps to determine whether the tumor is suitable for surgical resection or whether it would better be treated with chemotherapy, including trans-arterial chemo-embolization.
- ... by detecting the tumor earlier, improvement in the previously reported resectability rate could be achieved.



AIMS

To investigate the value of C-arm Lipiodol (ethiodized oil) injection computed tomography (CT) for intra-procedural hepatocellular carcinoma (HCC) lesion detection during transcatheter arterial chemoembolization (TACE).

Materials and Methods: Single center prospective study

40 patients (37 male, 3 female; mean age, 52.6 ± 12.5 years, age range: 25-82 years) diagnosed with HCC (words after sentence) All patients underwent 64-slice CT 1-2 wk before TACE.

- During the procedure, hepatic angiography was performed first. Following diagnostic embolization with Lipiodol injected into the hepatic artery, a C-arm CT scan was immediately conducted (C-arm Lipiodol CT). The CT scans were obtained 2 hours following Lipiodol® injection.

Results

- Preprocedural 64-slice CT detected a total of 13 suspicious lesions in the 40 patients.
- C-arm Lipiodol CT detected 71 lesions in total and Lipiodol CT confirmed 67 lesions with a diameter range of 3-12 mm.

Conclusion

C-arm Lipiodol CT has a higher diagnostic sensitivity for small HCC lesions. This technique may help physicians make intraprocedural decisions to provide patients with earlier treatment.

Safety

Common adverse events during use for HCC, may include fever, abdominal pain, nausea, and vomiting are the most common reactions; other reactions include hepatic ischemia, liver enzymes abnormalities, transitory decrease in liver function, liver decompensation and renal insufficiency. Procedural risks include vascular complications and infections.

IMPORTANT SAFETY INFORMATION CONTINUED¹

Indication and Usage

LIPIODOL® (ethiodized oil) injection is a prescription oil-based radio-opaque contrast agent indicated for:

- Hysterosalpingography in adults
- Lymphography in adult and pediatric patients
- Selective hepatic intra-arterial use for imaging tumors in adults with known hepatocellular carcinoma (HCC)

Contraindications

LIPIODOL® is contraindicated in patients with hypersensitivity to LIPIODOL®, hyperthyroidism, traumatic injuries, recent hemorrhage or bleeding.

- LIPIODOL® Hysterosalpingography is contraindicated in pregnancy, acute pelvic inflammatory disease, marked cervical erosion, endocervicitis and intrauterine bleeding, in the immediate pre- or postmenstrual phase, or within 30 days of curettage or conization.
- LIPIODOL® Lymphography is contraindicated in patients with a right to left cardiac shunt, advanced pulmonary disease, tissue trauma or hemorrhage, advanced neoplastic disease with expected lymphatic obstruction, previous surgery interrupting the lymphatic system, radiation therapy to the examined area.
- LIPIODOL® Selective Hepatic Intra-arterial Injection is contraindicated in the presence of dilated bile ducts unless external biliary drainage was performed before injection.

Warnings and Precautions

- Pulmonary and cerebral embolism may occur immediately or after a few hours to days from inadvertent systemic vascular injection or intravasation of LIPIODOL®. Avoid use in patients with severely impaired lung function, cardiorespiratory failure or right-sided cardiac overload.
- Anaphylactoid and anaphylactic reactions with cardiovascular, respiratory or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred following LIPIODOL® administration. Avoid use in patients with a history of sensitivity to other iodinated contrast agents, bronchial asthma or allergic disorders because of an increased risk of a hypersensitivity reaction to LIPIODOL®.
- LIPIODOL® hepatic intra-arterial administration can exacerbate chronic liver disease.
- Iodinated contrast media can affect thyroid function because of the iodide content and can cause hyperthyroidism or hypothyroidism.

Adverse Reactions

- Hysterosalpingography – Abdominal pain, foreign body reactions, exacerbation of pelvic inflammatory disease, salpingitis or pelvic peritonitis have been reported after the examination in case of latent infection.
- Lymphography – Lymphangitis, thrombophlebitis, edema or exacerbation of preexisting lymphedema, dyspnea and cough, iodism, allergic dermatitis, lipogranuloma, delayed healing at the site of incision.
- Selective Hepatic Intra-arterial Injection – Abdominal pain, nausea, and vomiting are the most common reactions; other reactions include hepatic vein thrombosis, hepatic ischemia, liver enzymes abnormalities, transitory decrease in liver function, liver decompensation and renal insufficiency. Procedural risks include vascular complications and infections.

Use in Specific Populations

- Pregnancy: The use of LIPIODOL® before or during pregnancy may interfere with thyroid function in both the pregnant woman and her fetus and may affect fetal development. Untreated hypothyroidism in pregnancy is associated with adverse perinatal outcomes, such as spontaneous abortion, preeclampsia, preterm birth, abruptio placentae, and fetal death. The use of LIPIODOL® before or during pregnancy causes iodide transfer across the placenta which may interfere with fetal thyroid function and may affect fetal development. Untreated hypothyroidism is also associated with increased fetal risk of low birth weight, fetal distress, and impaired neuropsychological development. Consider thyroid function testing during pregnancy if a woman was exposed to LIPIODOL® either before or during pregnancy, and also in infants whose mothers were exposed to LIPIODOL® before and during pregnancy or if clinically indicated.
- Pregnancy Testing: Confirm that the patient has a negative pregnancy test within 24 hours before LIPIODOL® administration for hysterosalpingography.
- Lactation: The use of LIPIODOL® may increase the concentration of iodide in human milk and may interfere with the thyroid function of the breastfed infant. Consider thyroid function testing in a breastfed infant whose mother was exposed to LIPIODOL® or if clinically indicated.
- Pediatric: For lymphography use a dose of minimum of 1 mL to a maximum of 6 mL according to the anatomical area to be visualized. Do not exceed 0.25 mL/kg. Administer the smallest possible amount of LIPIODOL® according to the anatomical area to be visualized.
- Geriatric: There are no studies conducted in geriatric patients.
- Renal Impairment: Prior to an intra-arterial administration of LIPIODOL® screen all patients for renal dysfunction by obtaining history and/or laboratory tests. Consider follow-up renal function assessments for patients with a history of renal dysfunction.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Lipiodol® is a registered trademark of Guerbet and is available by prescription only.

Please see the full prescribing information for additional important safety information.

References

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