GUIDELINES FOR ^{131}I - ETHIODISED OIL [LIPIODOL] THERAPY

I. PURPOSE

The purpose of this guideline is to assist nuclear medicine practitioners in:

1. evaluating patients who might be candidates for treatment using ^{131}I lipiodol for primary hepatocellular carcinoma.
2. providing information for performing this treatment
3. understanding and evaluating the sequelae of therapy

II. BACKGROUND INFORMATION AND DEFINITIONS

A. Definitions

1. ^{131}I is a beta emitting radionuclide with a physical half life of 8.04 days. The maximum and mean beta particle energies are 0.61MeV and 0.192MeV respectively. ^{131}I emits a principal gamma photon of 364 keV (81% abundance).

2. Ethiodised oil, also known as Lipiodol is a naturally iodinated fatty acid ethyl ester of poppy seed oil.

3. Therapy in this context means the intra-arterial administration of ^{131}I-Lipiodol.

B. Background

After hepatic intra-arterial injection, ^{131}I-Lipiodol follows arterial flow towards the tumour and is trapped in tumour microvessels. The remainder distributes in normal liver. 24hours post administration, 75-90% of administered activity is trapped in the liver. 10-25% pulmonary uptake results from arteriovenous shunting. After 24hours, tumour to normal liver uptake ratios range from 2.3 and 12. There is no recirculation. Tumour and normal liver effective half lives are 5.5 and 3.5 days respectively. A slight increase in lung activity occurs for 48 hours post administration, followed by a decrease with an effective half life of 4 – 5 days. Excretion is predominantly renal (30-50% within 7 days). Faecal excretion is low (3% in 5 days).

The therapeutic efficacy of ^{131}I-Lipiodol derives solely from radiation as opposed to the ischaemia associated with chemoembolisation. 90% of the radiobiological effect results from short range beta irradiation which favours destruction of tumour cells surrounding microvessels containing a high ^{131}I-Lipiodol concentration.

Physicians responsible for treating patients should have an understanding of the clinical pathophysiology and natural history of the disease processes, should be familiar with other forms of therapy and should be able to liaise closely with other physicians involved in managing the patient. The treating clinician should either see the patient jointly with the hepatologist or surgeon assuming overall management of the patient's condition or be prepared to assume that role. The treating clinician should be

appropriately trained and experienced in the safe use and administration of ^{131}I-Lipiodol therapy.

Clinicians involved in unsealed source therapy must be knowledgeable about and compliant with all applicable national and local legislation and regulations.

The facility in which treatment is administered must have appropriate personnel, radiation safety equipment, procedures available for waste handling and disposal, handling of contamination, monitoring personnel for accidental contamination and controlling contamination spread.

III COMMON INDICATIONS

1. Histologically confirmed, inoperable primary hepatocellular carcinoma.

CONTRAINDICATIONS

1. <u>Absolute</u>

   Pregnancy; breastfeeding
   Life expectancy less than 1 month
   Hepatic encephalopahy
   Tumour Stage OKUDA III
   Allergy to contrast media

2. <u>Relative</u>

Unacceptable medical risk for isolation
Unmanageable coagulation disturbance
Acute or severe chronic renal failure – creatinine clearance < 30 ml/min

IV PROCEDURE

A. Facility

The facilities required will depend on national legislation. The patient should be admitted to an approved isolation facility comprising an appropriately shielded room and en-suite bathroom facilities. The administration of ^{131}I-Lipiodol should be undertaken by appropriately trained medical staff with supporting scientific and nursing staff.

B. Patient preparation

Patients considered for ^{131}I-Lipiodol therapy will be ineligible for or will have failed conventional first line treatment.

Pre treatment assessment of tumour volume and serum tumour markers is essential.

C. Information for the procedure

Patients should receive both written and verbal information about the procedure prior to receiving

therapy. Informed written consent must be obtained from the patient.

D. Administration

1. ^{131}I-Lipiodol is supplied in solution for use at room temperature. Lipiodol is a viscous oil which offers high resistance to syringe dispensing and catheter injection. The radiopharmaceutical may be diluted with 2-10ml unlabelled lipiodol to increase the total volume of injection.

2. Stability data demonstrate < 5% free radio-iodine within 1 week of calibration at ambient temperature. Quality control checks are not usually required prior to therapy.

3. ^{131}I-Lipiodol should be prepared in an appropriately ventilated cabinet to avoid radio-iodine aerosol inhalation. Care should be taken to use Luerlock syringes and taps of a material which does not dissolve in lipiodol.

4. Treatment should be administered under safe aseptic conditions appropriate to intra-arterial injection in premises approved for unsealed source therapy. Hepatic artery catheterisation should be undertaken by appropriately trained interventional personnel.

5. The radiopharmaceutical is administered by slow intra-arterial injection under fluoroscopic control following conventional hepatic arteriography. The catheter is

positioned accurately depending on the vasculature and position of the tumour target(s). Tumour vascular access must be achieved without risk of systemic overspill via arteriovenous malformations or aberrant vasculature

6. A standard activity of 2.22 GBq (60mCi) ^{131}I-Lipiodol is injected slowly through a hepatic artery catheter via a protected glass or plastic syringe. The administered activity may be modified for medical reasons such as tumour load or according to local legislation.

E. Instructions for patients

1. The treating clinician must advise the patient on reducing unnecessary radiation exposure to family members and the public. Written instructions should be provided where required.

2. Following treatment, patients should avoid pregnancy for at least 4 months.

3. Patients should be advised of the potential side effects of ^{131}I-Lipiodol therapy

4. Nursing personnel must be instructed in radiation safety. Any significant medical conditions should be noted and contingency plans made in case radiation precautions must be breached for a medical emergency. Concern about radiation exposure should not interfere with the prompt appropriate medical treatment of the patient.

F. Precautions

Urinary ^{131}I excretion is of particular concern during the first 2 days post administration. Patients should be advised to observe rigorous hygiene to avoid urine contamination.

Usual arteriography precautions should be observed before and after the procedure including correction of clotting disorders and use of an arterial plug or compression bandage after catheter removal.

G. Radiopharmaceutical

Approved name: ^{131}I-Lipiodol

The radionuclide is supplied in solution for injection. The specific activity is 1.1 GBq/ml at calibration.

Radiation dosimetry:

Absorbed dose estimates for intra-arterial hepatic ^{131}I-Lipiodol administration

ORGAN	mGy/MBq
Liver tumour	43 +/- 22
Liver parenchyma	5 +/- 4
Lung	3 +/- 1
Gonads	0.5
Whole body	0.5

Note: data have been obtained in a particular patient group with hepatocellular carinoma and may vary with age and co-morbidity

Source: "Lipiocis et hepatocarcinome" monograph by CIS Biomedical

H. Guidelines for measuring the activity to be administered

The activity to be administered should be checked using an isotope calibrator.

I. Side effects

Early: Moderate pyrexia (29%)
Hepatic pain on injection (12.5%)
Self limiting respiratory symptoms (3%)
Acute pneumonitis (0.5%)

Delayed: Moderate, reversible leukopaenia (7%)

J Follow up

Quantitative whole body imaging one week post therapy is recommended to confirm the distribution of ^{131}I-Lipiodol. Local and whole body activity can be expressed as percentage of administered activity and compared with

an ^{131}I standard for dosimetry calculations.

V ISSUES REQUIRING FURTHER CLARIFICATION

1. The minimum / optimal time interval between repeated treatments.
2. Role of ^{131}I-Lipiodol in survival gain
3. Therapeutic potential of ^{131}I-Lipiodol for other tumour types.

VI CONCISE BIBLIOGRAPHY

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VII DISCLAIMER

The European Association of Nuclear Medicine has written and approved guidelines to promote the cost effective use of high quality nuclear medicine therapeutic procedures. These generic recommendations cannot be rigidly applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.

VII Description of the guideline development process

The EANM Radionuclide Therapy Committee has been involved in the process of guideline development for undertaking radionuclide therapies since 1995. A multinational group of therapy experts developed a series of monographs on the radioncuclide therapy

agents licensed for use throughout Europe. Subsequently a series of protocols was published on the Internet for use by members of the European Association of Nuclear Medicine. The monographs and protocols were achieved through a process of consensus taking note of the evidence available at the time of writing. The monographs and protocols have been in the public domain for four years and comments have been received from members of the nuclear medicine community. The guidelines have been developed using material within the monographs and protocols and have been formatted to harmonise with the Socety of Nuclear Medicine Therapy Guidelines format.

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