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TECHNICAL ASPECTS OF DOSIMETRY OF YTRIUM-90 IN TRANS-ARTERIAL TREAMENT OF LIVER CANCER AT CHORAY HOSPITAL

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Abstract

SIRT (Selective Internal Radiation Therapy)for liver cancer therapy is a method in which a dose of radiation was delivered millions of microspheres SIR-Spheres Ytrium-90 directly to liver tumors via hepatic artery.In this treatment, millions of tiny radioactive beads are injected directly into the arteries that supply blood to the tumour. These beads will stay in the blood vessels around the tumours. This allows a very strong radiation to reach the tumours directly. There is a very little effect on healthy parts of the liver or other tissues in the area such as intestines or skin.The treatment dose was limited less than the Maximum Treatment Activity (MTA) in order that the absorbed doses were not greater than the tolerances of normal liver (30Gy), of lungs (12Gy) and of bone marrow (1.5Gy)[1]. Clinical experiences gave the result: when combining with chemotherapy, radioactive microspheres can reduce the size of tumours better than using chemotherapy only. It can help to improve the quality of life and prolong the life of patients. For a large

Key words: SIRT (Selective Internal Radiation Therapy), liver cancer therapy, Ytrium-90, liver tumours.

number of patients, this treatment can also help to shrink tumours which can be removed later by surgery.

1. Introduction

According in Viet Nam, primary liver cancer is placed at the 3rd rank of mortality rate, behind lung cancer and stomach cancer. There are many ways to treat liver tumours, and we may be had a combination of treatments.Surgery is still the most popular method. However, the patient who cannot be treated by surgery (multifocal hepatocellular carcinoma, poor physical condition, liver failure due to cirrhosis or hepatocelluar carcinoma with invasive portal venous in progress or extra hepaticmetastasizes) were treated by SIRT method.

ChoRay Hospital have been researched a new study, millions of tiny radioactive Y-90 beads are injected directly into the arteries that supply blood to tumour. These beads will stay in the blood vessels around tumours. This allows very strong radiation to reach the tumours directly.

2. Physic Characteristic

The resin SIR-Spheres are labeled with ^{90}Y permanently bound to the device. Yttrium-90(^{90}Y) is a pure-beta emitter that decays to table Circonium-90 (^{90}Zr) with an average energy of 0.935 MeV via a half-life of 2.6684 days(64.2hrs), 94% of radiation delivered 11 days. The microspheres will distribute to the actively growing rim and provide radiation with an average range of 2.5mm and maximum in tissues of 11mm. SIR-Spheres microspheres consists of biocompatible microspheres designed to be average 35 μm (between 20-60μm) in diameter.The microspheres are supplied for single patient use with an activity of 3GBq $\pm$ 10% at the calibration time and date. SIR-Spheres microspheres are suspended in pyroxene free water for injection to a total of $\simeq$5ml per 3GBq (50Bq/microsphere) [2], [6].

Fig 1.SIR-Spheres Y-90 resin microspheres vial and microscopic view of the microspheres

The patient who is selected to treat by SIRT will be checked general health, including any signs of disease (such as lumps or weight loss) or anything else that seems unusual. The doctor will also take a history of health including past illnesses and treatments and will ask about patient's symptoms (about patient's illness, egg, tiredness, loss of appetite). Liver tumours can be diagnosed using a combination of blood tests and other diagnostic tests. Blood tests look at liver function and levels of tumour markers (certain substances which are linked to specific types of cancer). Liver tumours will often show on an ultrasound scan but full assessment requires a CT scan [3]. The patient will usually have a number of tests including: an angiogram, a scintigraphy scan (called a lung-shunting or MAA scan) and possibly, a special CT scan called a CT-hepatic angiogram.There are two methods for calculating the activity of SIR-Spheres microspheres to implant Empiric method (or BSA Method) and Partition model method. The main tasks of Medical Physics is calculating percent lung-shunting by SPECT/CT image (Tc99m-MAA) and selecting the methods for calculating method (BSA or Partition Model).

3.1 Shunting to the lungs:

High levels of implanted radiation by SIR-Spheres microspheres may lead to radiation pneumonitis. So that we have to check the amount of SIR-Spheres microspheres that has escaped through the liver and lodged in the lungs can then be expressed as the percent lung shunting.The percentage of shunting to the lungs is determined from a nuclear medicine scan usingtechnetium-99m labeled on macro aggregated albumin (Tc99m-MAA) for imaging. The TcMAA is injected via catheter placed in a similar manner to that which will be used to deliver theSIR-Spheres microspheres, that is, a trans-femoral catheter or surgically implanted catheter plus port placed into the hepatic artery at the time of the pre-treatment angiogram. The patient ispositioned under SPECT/CT machine and drawing ROIs (regions of interest) are defined as the liver and lungs. The activity of MAA particles that pass through the liver and lodge in the lungs can be calculated. And then the physicist calculated the T/N activity ratio (calculated as activity per unit mass of the organ or tissue) andpercentage lung shunting (or lung shunt fraction-LSF) [4]:

$$T/N = r = (A_{Tumour}/M_{Tumour})/(A_{Liver}/M_{Liver})$$

$$LSF = L = \frac{Lung\ counts}{Lung\ counts + Total\ liver\ counts} \times 100\%$$

If the percentage lung shunting is greater than 10%, activity of yttrium-90 may have to be further reduced. And if the percentage lung shunting is greater

than 20%, patients should not be treated by SIR-Spheres microspheres cause risk of radiation pneumonitis.

Furthermore, if the pre-assessment angiogram and MAA nuclear medicinescan demonstrates significant reflux of hepatic arterial blood to the stomach, pancreas or bowel,SIR-Spheres microspheres should not be implanted.

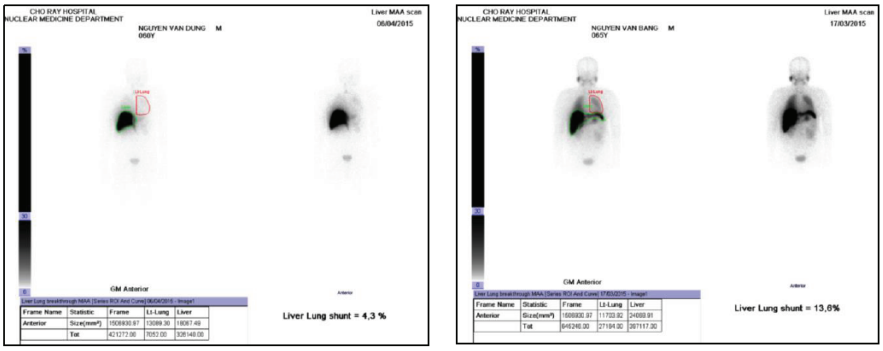

Fig 2: Liver-lung shunt calculation following scintigraphy with macro aggregated albumin (MAA). Using the geometric mean of ventral and dorsal images, the percentage of lung shunting can be determined from the total counts within ROIs over both lobes of the lung and the liver.

3.2 Dose Calculations

The preferred method for determining the prescribed activity of SIR-Spheres microspheres is the body surface Area (BSA) method. This method had been applied in many clinical studies in which SIR-Spheres microspheres have been used either alone or in combination with systemic chemotherapy. The BSA method adjusts the prescribed activity of SIR-Spheres microspheres to be implanted according to the size of the tumour within the liver and the size of the patient, with adjustment being made for the amount of the liver to lung-shunting in the particular patient. The appropriate volume and mass (whole liver or single lobe) are determiners using the CT or MRI images, assuming a conversion factor of 1,03g/cm^3[5].

The patient's Body Surface Area (BSA) to be calculated from the patient's weight and height. The percentage of the liver that is replaced with tumour as calculated from the CT scan, MRI,This process will take volume of tumour, volume of normal liver and volume of total. The percent lung shunting is calculated from Nuclear Medicine break-through scan, SPECT scan with Tc99m-MAA. The treatment dose was limited less than the Maximum Treatment Activity (MTA) in order that the absorbed doses were not greater than the tolerances of normal liver (30Gy), of lungs (12Gy) and of bone marrow (1.5Gy) [1].

The activity of Yttrium-90 being given to the patient is calculated by the following equation:

$$Activity\ of\ Y90\ (GBq) = (BSA(m^2) - 0.2) + \frac{Volume\ of\ tumour(m^3)}{Volume\ of\ total\ liver(m^3)}$$

BSA is calculated from a weight/height chart: [4]

$\mathrm{BSA(m^2)} = 0.20247\ \ \mathrm{height(m)}^{0.725}\ \ \mathrm{weight(kg)}^{0.425}$

If the partition model is used, then the radiation dose to the normal liver parenchyma should not exceed 80Gy in patients with normal liver and 70Gy in patients with cirrhosis.The dose to the lung should not exceed 25Gy. The dose received by the tumour has no upper limit. So that we have to calculate calculate the radiation dose received by an organ after SIR-Spheres microspheres have been delivered to that organ.

The tissue radiation dose that will be delivered to the normal liver and tumour can be calculated by formula [4]:

$$Tissue\ Radiation\ Dose\ (Gy) = \frac{49670 \times Total\ Y90\ activity\ in\ organ\ or\ tissue(GBq)}{Mass\ of\ the\ organ\ or\ tissue\ (g)}$$

If the percent lung shunting is more than 10% then the amount of SIR-Spheres microspheres delivered to the patient must be reduced.The percent lung shunting may alter the activity that can be safely implanted commensurate with acceptable risk of radiation pneumonitis. The following recommendations apply [4]:

Percent Lung Shunting	***Activity of SIR-Spheres microspheres***
<10%	Deliver full amount of SIR-Spheres
10% to 15%	Reduce amount of SIR-Spheres by 20%
15% to 20%	Reduce amount of SIR-Spheres by 40%
>20%	Do not give SIR-Spheres microspheres

The reduction in the activity implanted should be considered in light of the radiation dose thatmay be received by the tumour. In some patients, a reduction in activity of 20% may ensure thesafety of the lung, but no longer provide sufficient radiation to the tumour.

3. Result

The procedure is including in 6 steps:

1. **Angiogram**-providing a detailed picture of the blood supply to the liver(DSA room).
2. **Scintigraphy (lung-shunting scan or MAA scan)** - Determine the extent of lung shunting by Tc99m-MAA scan (Nuclear Medicine Department-NM)
3. The patient has another catheter placed in the artery in the groin. Like the first step, the catheter will be threaded to patient's liver (DSA room)
4. **Y-90 Infusion**- doing by an interventional radiologist, a doctor who specializes in treating liver tumors with minimally invasive procedures done using X-ray guidance (DSA room).
5. Disposal of radioactive waste (NM)
6. **"Bremsstrahlung"** scan - scanning SPECT after the treatment to confirm the placement of the microspheres (NM)

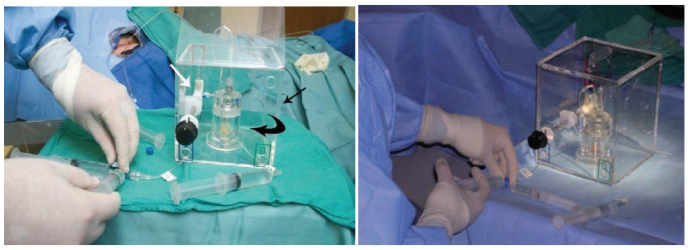

Fig3.The microspheres are delivered through the angiographic catheter directly into the hepatic artery branch supplying the liver tumour.

After SIRT treatment, the patient was monitored overnight at hospital. Sedative, antipyretic, proton puma inhibitors, corticosteroids, antibiotics are indicated to prevent fatigue and complications after the procedure. Clinical monitoring, blood count test, kidney and liver function test are required in the first 48 hrs [7].

Yttrium-90 is one of the most popular isotopes for this therapy. Its β-emission delivers a high and well located dose to the targeted areas. However, the verification of the isotope's position in the body is difficult due to its low gamma emission. The bremsstrahlung interactions between the emitted electrons and the body give rise to a continuous spectrum of photons that can be used for imaging. So that theMedical Physicist set the channel SPECT scan at 90keV, width window 60%, and collimator medium to confirm the placement of the microspheresin liver. Bremsstrahlung scan will be done about 30hrs after treatment.

SIRT with above physical characteristic and technicalhas been applied to many patients at Cho Ray Hospital is considered safe and effect.

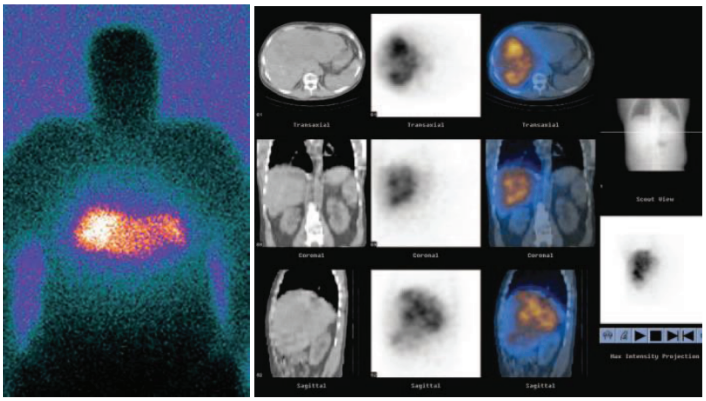

Fig 6. BremsstralungPlannar SPECT (right) and SPECT/CT (left) scanto confirm the placement of the microspheres in liver after treatment.

8 patients were included in this study, 7 males and 1 female. The mean age was 57.125 ± 9.014 years (range 39-65). We followed-up patients periodically every 02 months and through telephone. Eight patients had still surveyed after 04 months follow-up. One patient showed complete response with complete disappearance of the tumour after treatment.

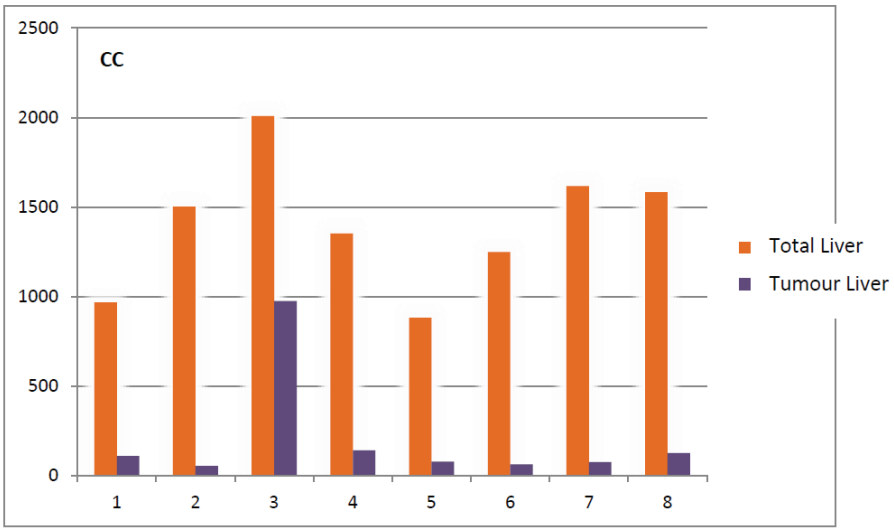

Fig 7. Volume's distribution of tumour liver per liver total

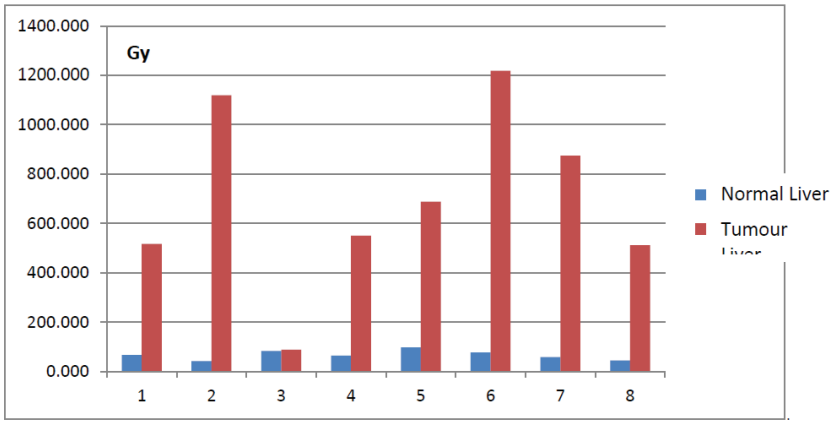

Fig 8. Distribution of dose for Normal liver and Tumour liver . The graph shows that the Ytrium90 dose providefor liver almost absorbed into the tumour liver tissue.

4. Conclusion

SIRT with Y90 is a safe and cost effective method to treat primary liver cancer. Larger numbers of patients are necessary to further evaluation and to promote a randomized comparative study of treatment efficacy between this method and the other treatment method (Surgical Resection, Chemoembolization, TOCE,). The procedures of quality assurance and radiation safety were carried out for all related facilities and techniques of radiation measurements. The method was applied on many patients of inoperable liver cancer at ChoRay Hospital and was evaluated safety, effective and feasible by research group of ChoRay Hospital in their common reported articles.

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