A Preparation of ^{113m}In Sulfur Colloid for Bone Marrow and Liver Scanning

Tsutomu Mishima, M.D. and Kin-ichi Hisada, M.D.
The Department of Radiology, School of Medicine, Kanazawa University, Kanazawa, Japan
(Chief: Prof. Hiroshi Hiramatsu)

骨髄および肝スキャンニング用としての ^{113m}In sulfur colloid 法

金沢大学医学部放射線医学教室（主任　平松　博教授）
三　嶋　　勉　　久　田　欣　一

（昭和44年10月25日受付）

^{113m}In colloid を使用するヒトの肝および骨髄等の網内系スキャンニングでは，肝の Radiation dose が非常に少なく，従つて比較的安全に大量投与ができ鮮明な imageが得られる．特に最近その有用性が認識されてきた骨髄スキャンニングには，大量のＲＩを必要とする点で，^{113m}In のごとき短半減期核種の colloid 製剤は欠くことのできぬものである．^{113m}In colloid 調製法はすでにいくつかの方法が報告されているが著者らは，チオ硫酸ナトリウム，^{113m}In 溶液，ゲラチンの混合液を加熱することによつて形成される ^{113m}In sulfur colloid 法を確立した．これは，オートクレーブ滅菌が可能であり，肝摂取率は82％（Rat）と高く安定した colloid である．ＲＥＳに貪喰される colloid は，ほとんど体外に排泄されないが，^{113m}Inでは物理的半減期が非常に短いため，例えば10mCi の ^{113m}In sulfur colloid を投与しても24時間後には1μCi 以下となり，翌日の他のＲＩ検査にほとんど障害にならない．この点は，^{99m}Tc colloid にまさるもう一つの長所である．

In organ scannings a large dose of short-lived radioisotope increases the photon output and makes possible to achieve images of high quality. In addiation, with the scintillation camera multiple views of an organ can be obtained routinely and even stop motion scintiphotographs are feasible avoiding respiratory movements.

The advantage of colloidal preparations labeled with short-lived nuclides, such as ^{113m}In or ^{99m}Tc, is that large doses can be used for scanning of the reticuloendothelial system i.e. the liver, spleen and bone marrow, because of the low absorbed radiation dose to the patient. The preparation of ^{113m}In colloid for liver scanning has been reported by Goodwin et al[1]. The present authors searched for a simpler and more efficient method of preparing colloidal ^{113m}In and developed a ^{113m}In sulfur colloid using a reaction of sodium thiosulfate with ^{113m}In. This new radiopharmaceutical was evaluated clinically especially for bone marrow scanning. The methods of preparation and some results are reported.

Preparation of ^{113m}In Sulfur Colloid

1) ^{113m}In was eluted with 6 ml of dilute hydrochloric acid (pH 1.5) from a 50 mCi ^{113}Sn-^{113m}In generator and was transfered to a 20 ml vial.

2) 20% gelatin solution was added to the eluate in the vial so that the final gelatin concentration

was 1 mg/ml.

3) Next, 1.5 ml of 0.02 M $Na_2S_2O_3$ (sodium thiosulfate) solution was added.

4) The mixture was heated in a boiling water bath for three to five minutes until its appearance became opalescent.

5) After 1 ml of sodium phosphate buffer solution was added, the preparation was cooled by tap water.

6) Using a pH-meter, the solution was adjusted to pH 7.0 with 1 N NaOH. The total preparation time was less than ten minutes.

7) Prior to injection, the final production was sterilized by autoclaving at 15 psi for twenty minutes until it became clear.

Organ Distribution of ^{113m}In Sulfur Colloid

For a study of the distribution of the colloid in the various organs of rats, animals were sacrificed thirty minutes after its intravenous injection and the radioactivity in each organ was measured separetely with a scintillation counter. The results expressed as per cent of the administered dose are shown in Table 1. The concentration of the ^{113m}In activity was 82% in the liver and 1.6% in the spleen. A low

Table 1. Distribution of ^{113m}In sulfur colloid in rats thirty minutes after intravenous injection

Organs	Dose (%)	average of three rats
Liver	82.0	
Spleen	1.6	
Kidneys	0.9	
Lungs	0.5	

concentration of ^{113m}In activity in the lungs indicates the abscence of macroaggregated impurities. The remaining activity was taken up mainly in the other RES including bone marrow.

Clinical Results

Figure 1 shows a liver scan with one mCi of ^{113m}In sulfur colloid fifteen minutes after intravenous injection using a 3-in. diameter NaI (Tl) scanner. The quality of the scan is satisfactory and the spleen can also be seen distinctly. Chronic hepatitis was suspected in this case.

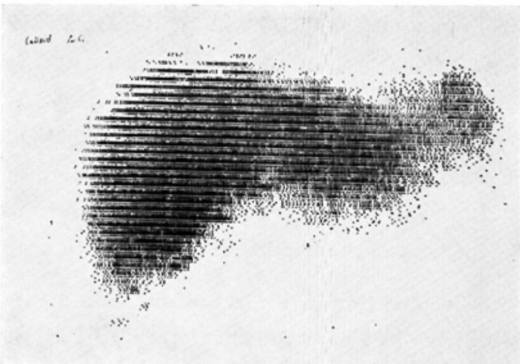

Fig. 1. Liver scan (T.M. 51y) made with 1 mCi of ^{113m}In sulfur colloid 15 minutes after intravenous injection.

Figure 2 shows a normal bone marrow scan of the pelvic region obtained with ten mCi of ^{113m}In sulfur colloid, forty-five minutes after intravenous injection, using a dual 3-in. diameter NaI (Tl) isosensitive scanner[2]. With such a large dose of ^{113m}In, an excellent scan of the bone marrow could be obtained in cases with normal bone marrow function.

A whole-body linear scan of the same patient is shown in Figure 3. The picture represents a distribution which corresponds to that of the RES in man.

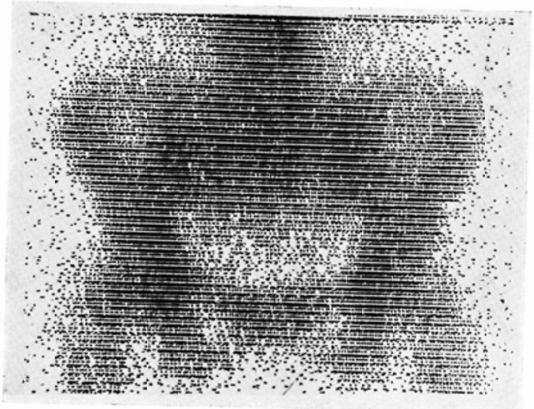

Fig. 2. Normal bone marrow scan of the pelvis (K.I. 59y) made with 10mCi of ^{113m}In sulfur colloid 45 minutes after intravenous injection.

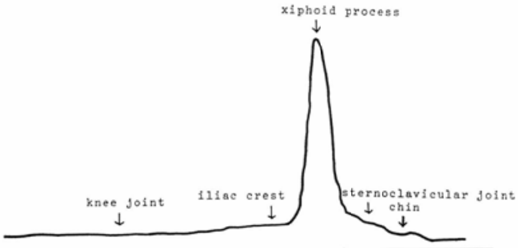

Fig. 3. Whole body linear scan of the same patient shown in Fig. 2.

Radiation Dose and Toxicity

The absorbed radiation dose to the liver was estimated to be 0.55 rads per mCi of ^{113m}In[1].

In this respect, ^{113m}In sulfur colloid is the most suitable agent for bone marrow scanning since the radiation dose to the liver as the critical organ is low, although a large amount of radioactivity is required for bone marrow scanning. Sulfur colloid was used intravenously previously during the 1930 for the treatment of arthritis with repeated single injections of 1–30 mg and these amounts proved to be nontoxic[3]. The toxic dose in small animal was observed as 30–40 mg per kilogram of body weight[4]. For scanning, the amount of sulfur colloid administered to the patient in a single injection is less than 1 mg.

Dissucussion

The method of preparation of the ^{113m}In sulfur colloid is rapid and simple. The reaction of sodium thiosulfate with $^{113m}In^{+++}$ in acid solution may produce $^{113m}In_2S_3$. This compound can not be completely precipitated chemically, even though it is insoluble in water, because the amount of ^{113m}In in solution is extremely small. Much of the sulfur colloid is produced from the thiosulfate and hydrogen ions in solution. We asume that the $^{113m}In_2S_3$ combines strongly with the non-radioactive sulfur colloid forming a stable and complete ^{113m}In sulfur colloid. The biological behavior of this preparation in animals and man supports the assumption of the formation of a suitable radioactive colloid. A high liver concentration of ^{113m}In was observed in our preliminary experiments without use of a sodium phosphate buffer. Consequently, in preparation of the ^{113m}In sulfur colloid, sodium phosphate is not necessarily required.

The absorbed radiation dose to the liver was calculated to be 5.5 rads for 10 mCi of ^{113m}In sulfur colloid used for bone marrow scanning. The same dose to the liver is obtained per 150 μCi of ^{198}Au colloid used for conventional liver scanning[5]. However at least 1 mCi of colloidal ^{198}Au would be required for a bone marrow scanning.

Because of the 1.7 hr. half-life of ^{113m}In, the activity of ^{113m}In remaining in the whole-body will be found less than 1 μCi at twenty four hours after administration of 10 mCi of ^{113m}In sulfur colloid assuming no excretion. Therefore other radioisotope studies the following day will not be affected by the previous scanning. This is one of the advantages of ^{113m}In sulfur colloid over ^{99m}Tc colloid with a half-life of 6 hrs.

Summary

^{113m}In sulfur colloid was prepared for scanning of the RES in man. This agent can be produced rapidly and easily by heating a mixture of sodium thiosulfate, ^{113m}In eluted from a generator with HCl of pH 1.5 and some gelatin.

Liver concentration of ^{113m}In sulfur colloid in rats was 82%. Liver and bone marrow scans were carried out with good result in man and low radiation dose. The preparation was found to be most suitable for bone marrow scanning.

Acknowledgment

The authors wish to thank Prof. H. Hiramatsu for his constant interest and guidance in this investigation.

Department of Radiology
School of Medicine
Kanazawa University
Takara-machi 13-1
Kanazawa, Japan

References

1) Goodwin, D.A., Stern, H.S., Wagner, H.N., Jr. and Kramer, H.H.: A New Radiopharmaceutical for Liver Scanning. Nucleonics 24(11), 65, 1966.
2) K. Hisada, S. Ohba and M. Matsudaira: Isosensitive Radioisotope Scanning. Radiology 88, 124, 1967.
3) Comroe, B.I.: Sulphur Therapy in Arthritis with a Review of the Literature. Medicine 18, 203, 1939.
4) Wheeldon, T.F. and Main, R.J.: The Use of Colloidal Sulphur in the Treatment of Arthritis. J. Bone and Jt. Surg. 15, 94, 1933.
5) Quimby, E.H.: Some Problems Regarding Permissible Dose with Radioactive Isotopes. J. Nuclear Med. 7, 817, 1966.