



Title	Contrast visualization of lymphatic system with lipiodol ultra-fluide (Ethiodol)
Author(s)	鈴木, 慎二; 高野, 竹生; 奥島, 仁太郎
Citation	日本医学放射線学会雑誌. 1964, 24(3), p. 275-283
Version Type	VoR
URL	https://hdl.handle.net/11094/15763
rights	
Note	

The University of Osaka Institutional Knowledge Archive : OUKA

<https://ir.library.osaka-u.ac.jp/>

The University of Osaka

CONTRAST VISUALIZATION OF LYMPHATIC SYSTEM WITH LIPIODOL ULTRA-FLUIDE (ETHIODOL)

By

Shinji SUZUKI, Takeo TAKANO and Jintaro OKUJIMA

Department of Radiology, School of Medicine, Keio University

(Director: Prof. H. Haruna)

Lipiodol Ultra-Fluide (Ethiodol) によるリンパ系造影について

慶大医学部放射線医学教室（春名英之教授）

鈴木 慎二 高野 竹生 奥島仁太郎

（昭和39年 4 月28日受付）

リンパ系造影は悪性腫瘍の診断・治療などに関して、重要な検査法の一つである。殊に触診その他の検査で診断の出来ない骨盤腔及び後腹膜リンパ節における、原発及び転移性腫瘍の診断には欠くことの出来ない検査法である。

私達は各種悪性腫瘍20例、乳糜尿4例の計24例に対して、造影剤 Lipiodol Ultra-Fluid (Ethiodol) を使用して、リンパ系造影を行った。

造影法は Kinmonth 法を多少改良して行つた。造影によるX線所見の分類は、（1）造影剤の通過時間、（2）リンパ管の数及び太さの異常、

（3）リンパ管の分布の異常（異常径路によりリンパ流）、（4）リンパ節の変位、（5）リンパ節の大きさ及び形の異常、（6）リンパ節内部構造の異常（陰影欠損及び異常充盈）とした。

造影による副作用としては、発熱・肺の脂肪栓塞・肺毛細気管支炎などであり、ヨード過敏症もみられた。しかし重篤な例は一例もなかつた。これらの副作用は造影剤の注入時間と注入量に関係がある。私達は体重1kg当り0.1～0.3ml、以下の量を使用し、注入所要時間は5～7ml/h.、即ち2～3時間をかけて注入している。

Introduction

The contrast procedures of the lymphatic system are classified into lymphangiography and lymphography. Lymphangiography is applicable to the diagnosis of chronic edema of the limbs whereas lymphography is applicable to the diagnosis of various kinds of malignant tumors and haematic diseases. However, any contrast media injected into the lymphatic will flow into the blood circulation definitely through some lymph glands and the thoracic duct. The primary object of contrast procedure of the lymphatic system for application to the diagnosis of malignant tumors is to diagnose the lymph glands in the pelvis or para-aortic glands which cannot be diagnosed by palpation.

Contrast Procedures

The contrast procedures consist of a direct method and an indirect method. Hudack et

Table 2 Contrast procedure of lymphatic system

1. Disinfection of feet and hands
2. Colouring of lymph
0.3—0.5 ml of a mixture of 5% Patent blue solution and 1% Novocain liquid injected into between the toes subcutaneously (between the 1st and 2nd toe.)
3. 5-10 minutes after the injection the skin around the coloured lymph canal is cut open and the lymph canal exposed.
4. 27 gage needle with a polyethylene tube is thrust into the lymph canal and ligament fixed.
5. Anti-cancer, Endoxan 50 mg is dissolved in a solvent 5 cc and the resulting solution injected into the lymph canal.
6. Contrast medium injected. (in 1-2 hours)
By the use of a slender tube under contrast pressure (manufactured by Itonaga Medical Instrument Co., Ltd., Japan)
7. After Completion of the injection, the needle is with drawn and the skin sutured.
8. Roentgenography
 - 1) Completion of injection (within 10-30 minutes)
The lymph canal, lymph glands and thoracic duct can be visualized.
 - 2) 12-24 hours after procedures, the lymph glands only can be seen.
 - 3) 1-4 months later, the lymph glands only can be seen.
9. Sulfamine is administered for 3 days.

so that through a slender needle is used in intralymphatic canal injection, the injection is easy to handle, excellent in providing clear contrasts. However, the contrast medium remains in the lymph gland only for a period within 24 hours. thus proving itself insufficient for an observation of the progress of the patient and showing no detail of the internal structure, i.e. the reticular structure so that the lymph gland can be contrasted only as a homogenous entity. In this manner, aqueous contrast media are considered unsuitable for the purpose of contrast of the lymph glands, though some good results there by can be achieved in cases of the lymph canals (lymphangiography).

In contrast, oily contrast media can be changed to fat drops filling the reticular system of the lymph glands so that they come to show a so-called contrast of the reticular like (a general uniform small mark shadow) and moreover, they remain in the lymph glands for even 3-4 months there by benefiting the observation of the patient's progress and the internal structure. However, it cannot be denied that their concentration in roentgenography is still poorer than that of aqueous contrast media, because of a less content of iodine than the latter and moreover, the former is rather difficult to inject because of their high viscosity.

By investigating literature of the past where lymphatic contrast media are employed, we can find Thorotrast, Joduron, Triopac, mercury solution (for animal) and Hypaque. While all test media are aqueous solution, it was Jackson et al⁴⁾ who used Ethiodol in 1961 and since that time almost everybody seems to have used Ethiodol as found in the liter-

ature thenceforward.

Further recently, though different from contrast media, such radioactive isotopes have been also used as ^{177}Lu , ^{198}Au , RIHSA etc as well as such radiolymphography as by means of uptake of the lymph glands or scintigram.

Ethiodol is understood to be the trade name of Lipiodol Ultra-Fluide in U.S.A.

As is already well known, Lipiodol was firstly used by Sicard and Forester as an oily contrast medium in 1921. By the way, this preparation is an organic compound composed of iodine and poppy seed oil. However, as is shown in Table 3, because of its high viscosity, approx. Five times as large as that of glycerin, it is difficult to inject into any slender tract.

Lipiodol Ultra-Fluide (abbreviated as Lipiodol U.F. hereinafter) is a light yellowish oily liquid in which iodine is organic-bound to the fatty acid ethyl ester to lower its viscosity. The content of iodine is 38% w/v at a saturated concentration, namely, 1 ml of this liquid contains iodine 0.48 g. Its viscosity is approx. 65 c.p.s. at 15°C.

This oily contrast material injected into the lymph of back of the foot is destined to take the course of the lymph of the lower thigh→deep inguinal lymph glands→iliac lymph glands→lumbar lymph glands→para-aortic lymph glands→Cisterna chyli→thoracic duct→jugular vein→heart→Pulmonary artery→lung. In other words, since the contrast material infiltrates into the vascular system in the long run, it is necessary to limit its amount for injection. In this regard, we usually make it a rule to resort to the following standard.

Dosage (For adult: Below 0.3 ml/kg body weight)

Unilateral upper limb: 5-10 ml

Unilateral lower limb: 10-15 ml

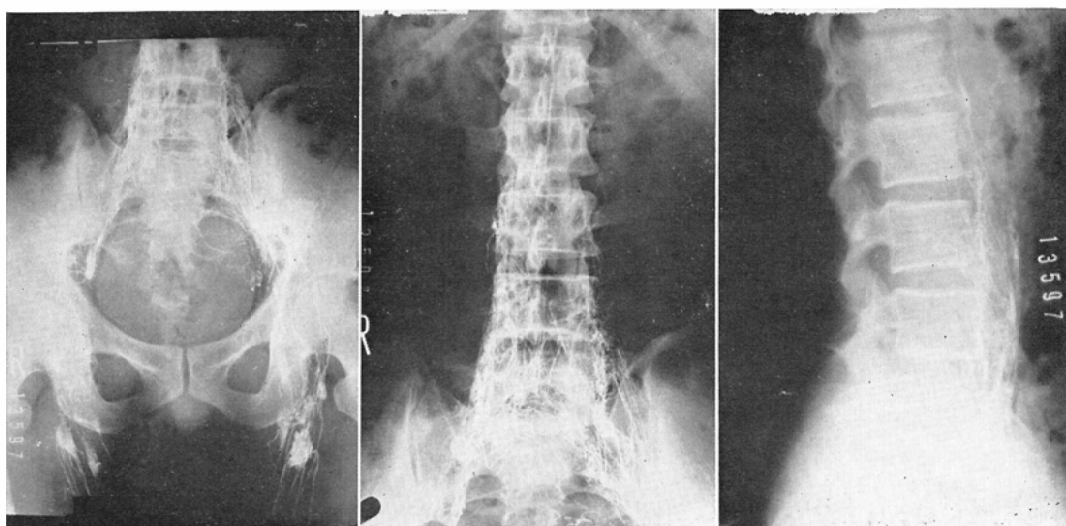
Bilateral lower limb: 15-20 ml

Rate of injection:

Small amount injecting apparatus under
constant pressure (motor-type)

Table 3 Properties of Lipiodol Group

	Lipiodol	Lipiodol F	Lipiodol U. F.
Property	Iodized poppy seed oil fatty acid glycerin ester	Mixture of iodized poppy seed oil fatty acid ethyl ester and glycerin ester	Iodized poppy seed oil fatty acid ethyl ester
Content of Iodine	37.0-42.0% 0.54g/ml.	40% 0.52g/ml.	38% 0.48g/ml.
Specific Gravity at 15°C	1.350	1.315	1.280
Viscosity at 15°C (cps)	1,800	250	65



Case No. 2 I.T. Male 41 years old. Diagnosis: Seminoma.

Lipiodol U.F. 30 ml/2.5 hours injected into the back of both feet. Side effects: Fever and Cough.

Findings: Almost all parts of the iliac and para-aortic lymph glands previously subjected to radiation of large amount of Co^{60} were contracted, but an apparent increase in the number of the lymphatic canals could be noted. There is no relapse or metastasis of the disease and the patient is now in healthy condition.



(a)



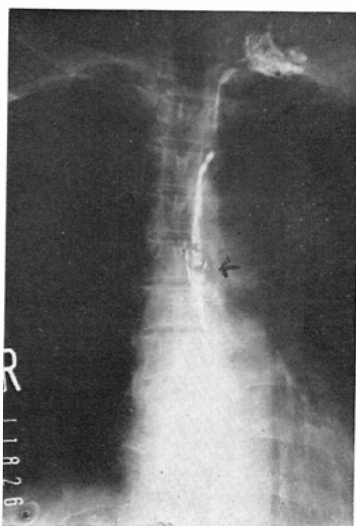
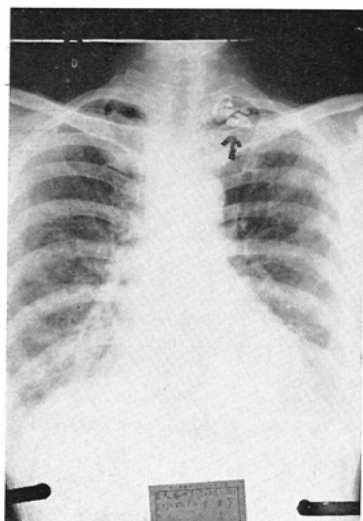
(b)

Case No. 10 S.K. Female 19 years old. Diagnosis: Chyluria.

Lipiodol U.F. 18 ml/2.5 hours injected into the back of the right foot. Side effects: None.

Findings: (a) By means of regressive pyelography, back-flow of the contrast material is noted from the calyx to the lymph.

(b) By means of lymphangiography a large number of lymph canals are seen communicating with the calyx. Although the contrast material was injected into the back of the right foot in the case, there was noted back-flow of the contrast material in the lymph canals of the left ilium, but the thoracic duct showed a contrast.



Case No. 1 K.O. Female 62 years old. Diagnosis: Carcinoma of rectum.
Lipiodol U.F. 25 ml/2.5 hours injected into the back of both feet. Side effects:
Slight fever, cough and dyspnea.

Findings: Discovery of metastasis in the lymph glands of the left external ilium. Interrupted shadow of the thoracic duct (←). Swelling of the left Virchow's gland (↑). Shadow of bronchiolitis in both lungs are apparent.



Case No. 12 M.T. Female 46 years old.
Diagnosis: Postoperative metastasis of uterine cancer. Lipiodol U.F. 18 ml/2.5 hours injected into the back of both feet. Side effects: None.
Findings: Fist-size swelling was palpated in the left pelvic cavity. Immediately, deep X-ray therapy was performed. Stores of the contrast material were noted in the same site (arrow referred to). This is considered to be necrotic softening inside the swelling.



Case No. 18 H.K. Female 62 years old.
Diagnosis: Postoperative condition of uterine cancer. Lipiodol U.F. 17m/2.5 hours injected into the back of both feet. Side effects: None.
Findings: No relapse or metastasis clinically. No metastasis of the lymph glands. Part of the iliac lymph glands and collateral channel is noted in the lymph canals.

Clinical Application

During the past two years, we have carried out lymphangiography and lymphography in approx. 100 cases for the purpose of achieving the objects shown in Table 4. Out of this figure, 24 cases were treated with Lipiodol U.F. as summarized in Table 5. Still out of these 24 cases, respective findings were obtained in 18 cases. On the basis of these findings, the patients underwent radiology or operative therapy and are now under observation still in progress.

As for classification of pathological findings, we also make it a rule to observe the following.

1. Time of passage of contrast media.
2. Number of lymph canal and abnormality in size of lymph canal.
3. Abnormality in distribution of lymph canals (lymph flow due to abnormal path).
4. Abnormality in position of lymph glands.
5. Abnormality in size and shape of lymph glands.
6. Abnormality in internal structure of lymph glands (defect of shadow. Abnormal filling).

Recently, a few reports have been noted on the availability of oily contrast media coloured with chlorophyll or the like just before surgical operation for contrast purpose of the lymphatic system so that an extraction of the lymph glands can be facilitated in a convenient manner. We have also utilized this procedure in a few cases only to find that the colouring effect of chlorophyll lasts a comparatively short period, thus giving us no significant value.

In case such colouring is required, Patent blue has only to be subcutaneously injected between the toes 10-20 minutes before operation, thus enabling sufficient purpose to be ascertained.

Table 4 Objection of Lymphography

1. Indications :	
Benign diseases	Lymphangioma, Chronic edema, Elephanciasis, Chyluria
Malignant diseases	Malignant lymphoma, Lymphatic leucaemia
	Lymph metastasis of malignant tumors
2. Clinical application :	
1)	Diagnosis for various types of diseases.
2)	Diagnosis for progress of malignant tumor.
3)	Indication of extracting scope of lymph glands.
4)	Decision of position for X-ray irradiation.
5)	Adjudication of treatment efficacy.
3.	Application of treatment that injects anti-tumor agent into lymph canal.

Side Effect

The side-effects due to injections of Lipiodol U.F. are summarized in Table 5. The

main side-effect are fever and cough, the former occurring rather frequently in our cases. This trend can be seen in many cases treated with a large dosage of the contrast material, and the cause of this kind of fever is by no means an infections one due to bacteria, but may be due to some foreign matter or impurities. Although fever lasts a few days, it usually disappears very soon with the use of an ice pillow or the like. Coughing is also only transitory in most cases, thus involving no particular problem.

As for iodine hypersensitivity, it is quite essential to test the patient in that sense before injection. Besides, fatty embolism or bronchiolitis of the pulmonary due to the injection of a contrast material can be sometimes observed as complications. Eventually, a small amount of phlegm mixed with blood may occur. However, we have never experienced even a single case subjected to any side-effects under our treatment. Looking into some literature of side reactions, we find that Wallace et al⁵⁾ have observed out of 110 cases 2 cases of lymphangitis, 3 of cut infection, a few cases of pulmonary fatty embolism and 6 cases of fever. Baron et al⁶⁾ reported on oil embolism due to Ethiodol and Fuchs

Table 5 Cases of contrast visualization of lymphatic system with Lipiodol U.F.

Case No.	Sex: Age	Diseases	Amount of Lipiodol U.F. (ml)	Site of injection	Side-effects		
					fever	cough	others
1.	female 62	ca. of rectum	25	both feet	*+	+	slight dyspnea
2.	male 41	seminoma	30	both feet	**+	+	
3.	ma. 65	ca. of penis	25	both feet	+	—	
4.	ma. 29	malignant struma	20	both feet	—	—	
5.	ma. 58	ca. of tonsill	18	left foot	—	—	
6.	ma. 59	malignant lymphoma	25	both feet	—	—	Dermatitis (iodine reaction)
7.	ma. 61	malignant lymphoma	22	both feet	—	—	Dermatitis
8.	ma. 57	ca. of urinary bladder	18	both feet	—	—	
9.	ma. 71	ca. of rectum	10	right foot	+	—	
10.	fem. 19	chyluria	18	right foot	—	—	
11.	ma. 69	ca. of prostate	18	right foot	—	—	
12.	fem. 46	ca. of cervix uteri	18	both feet	—	—	
13.	ma. 54	chyluria	18	left foot	—	—	
14.	fem. 43	ca. of rectum	18	both feet	—	—	a small amount of blood phlegm
15.	ma. 68	malignant lymphoma	15	both feet	—	—	
16.	ma. 42	ca. of rectum	18	both feet	—	—	
17.	ma. 35	ca. of rectum	18	both feet	—	—	
18.	fem. 62	ca. of cervix uteri	17	both feet	—	—	
19.	fem. 45	chyluria	18	left foot	+	—	
20.	fem. 67	ca. of cervix uteri	18	left foot	+	—	
21.	fem. 71	ca. of rectum	18	both feet	—	—	
22.	fem. 59	ca. of cervix uteri	18	both feet	—	±	
23.	ma. 64	chyluria	17	left foot	—	—	
24.	fem. 64	ca. of cervix uteri	18	both feet	—	—	

* under 38°C ** over 38°C

et al⁷⁾ also reported on pulmonary infarction and cardiovascular collapes.

We have found 7 cases of fever, 4 cases of cough, 2 cases of dermatitis, each case of slight dyspnea and small amount of phlegm mixed with blood, among all the cases under our own treatment. However, fever disappeared almost in a couple of days by means of and ice pillow or the like and coughing was noted only after the contrast procedure, thus requiring no special treatment. No single case of lymphangitis was seen. As for after-disorders, we have encountered a few cases since we started contrast media procedure more than one and a half years ago, but none of any apparent after-disorders has been noted.

Conclusion

The contrast procedure of the lymphatic system is regarded as very valuable in diagnosing or treating especially malignant tumor. As a matter of fact, this method has been utilized in various parts of Japan.

We have also conducted this procedure for contrasting the lymphatic system during the past two years, and reported on its method and the contrast material, Lipiodol U.F., as seen in various investigations, is found satisfactory in all points of viscosity, radiopacity, and side-effects. However, when using any oily contrast media for lymphangiography or lymphography, full circumspection should be employed in regard to careful selection of indications and the amount of contrast media for use. In fact, a slightly high rate of fever has been noted in the present report, which is considered due to overdosage of the contrast material. Therefore, we are using 0.1-0.3 per kg body weight at present. (Many thanks are due to Prof. Dr. H. Haruna for his guidance and inspection of the present report. We also appreciate generous supply of Lipiodol Ultra-Fluide from Kodama Shoji Co., Ltd.)

References

- 1) Hudack, S.S., & McMaster, P.D.: J. Exper. Med. 57 : 751, 1933. —2) Kinmonth, J.B., & Tayler, G.W.: Ann. Surg. 139 : 129, 1954. —3) Kinmonth, J.B. et al.: Brit. J. Surg. 45 : 1, 1957. —4) Jackson, L., et al.: Ann. Inter. Med. 54 : 370, 1961. —5) Wallace, S., et al.: Radiol. 76 : 179, 1961. —6) Baron, K.M., et al.: Radiol. 80 : 194, 1963. —7) Fuchs, W.A.: Acta Radiol. 57 : 427, 1962.