ACTA OBST GYNAEC JPN Vol. 31, No. 4, pp. 499–507, Apr. 1979

DIFFERENTIAL DIAGNOSIS IN GYNECOLOGICAL LESIONS BY COMPUTERIZED TOMOGRAPHY AND THE SIGNIFICANCE OF CONTRAST ENHANCEMENT

Kazuyuki TAKEICHI

Department of Obstetrics and Gynecology, Fukushima Medical College, Fukushima
(Director: Prof. Tsutomu Fukushima)

Synopsis The present study was undertaken to assess the value of computerized tomography in the diagnosis of lower abdominal tumors encountered in gynecological practice, especially the utility of contrast enhancement in the differential diagnosis of these disorders.

Various pelvic-abdominal tumors were scanned by means of a delta scanner and radiological densities of the lesions were measured in terms of delta number and compared. The results indicate that there is a definite relationship between the histopathologic nature of the tumor and the delta number.

However, it was shown that plain scan (pre-contrast scan) does not permit differentiation between solid and cystic ovarian tumors when there is an overlapping of their delta numbers.

The data also indicate that a linear relationship exists between the concentration of Urografin, the contrast agent used, and the delta number of scanned tumors, 100 mg/dl iodine corresponding to a delta number of 32.5.

Two methods of Urografin administration, i.e., bolus injection and biphasic infusion, were evaluated for their adequacy for radiodiagnostic purposes. Of these two, the latter, especially the method of 50 ml Urografin injected intravenously with subsequent drip infusion of 50 ml in 20 minutes, was found to be most adequate for the maintenance of the concentration of iodine in the blood.

A study of the time course of the delta number of solid ovarian tumor and uterine myoma, as measured on scans made after the administration of the contrast medium, showed that the value became nearly constant from 5 minutes after starting infusion onward. Hence, it seemed worthwhile to determine the delta numbers of the various tumors both before (pre-contrast scan) and more than 5 minutes after the infusion of contrast medium (post-contrast scan) and to compare the ratios of these two values (attenuation enhancement ratio or A.E.R.). The A.E.R. was estimated to be 1.75±0.2 for uterine myoma, 2.04±0.2 for solid ovarian tumor and 3.52±0.5 for choriocarcinoma, while corresponding values for ovarian cyst, hydatidiform mole and missed abortion all approximated to 1.0.

The contrast enhancement technique utilizing an appropriate contrast medium thus rendered it possible to make a differential diagnosis, for example, of solid vs. cystic ovarian tumors which tend to give an identical value of delta number on pre-contrast scan.

Key words: CT in gynecological lesions

Introduction

In neoplasms of gynecologic structures, notably lower abdominal tumors, an early correct differential diagnosis is of cardinal importance for the proper evaluation of prognosis as well as for the determination of therapeutic policy.

Strenuous efforts are currently being made to enhance diagnostic efficiency in these conditions. Various diagnostic procedures, e.g. hystero-salpingography (HSG), pelvic angiography (PAG), culdoscopy and laparoscopy, have been in popular use as valuable adjuncts to bimanual pelvic examination which is still a basic diagnostic tool. However, many of these procedures are not easy to perform and, moreover, are distressing and even hazardous to the patient.

In order to eliminate these drawbacks ultrasonic tomography and computerized tomography (CT) lately have been put into clinical use.

We devised a still less time-consuming, reliable auxiliary radiodiagnostic method involving CT and have used it in a number of patients with lower abdominal tumor with an enhanced accuracy of diagnosis[5]. In the present investigation we measured the radiological density of various lower abdominal tumors of women by means of computerized tomography and further studied the diagnostic significance of contrast enhancement.

Material and Methods

Subjects: A total of 78 cases were involved in this study. This series comprised 40 cases of ovarian tumor, 22 cases of uterine myoma, 3 cases of carcinoma corporis uteri, 3 cases of missed abortion, 4 cases of hydatidiform mole and 6 cases of chorio carcinoma.

In a separate group of 15 healthy volunteers serial measurements were made of the iodine concentration of blood before and after the intravenous injection of a contrast medium (60% Urografin).

Methods: The computerized tomography was performed with a delta scanner (Ohio-Nuclear Ltd.; 256×256 convolution based algorithm); the X-ray tube was operated at 120 kV and 30 mA, each scan time was 2.5 min. This scanner is of outstanding diagnostic use since the radiological density at any place in the scan image it produces can readily be given as the delta number by the use of a Joy-stick.

I. Comparison of delta numbers of various tumors

1) All patients were measured for the preoperative delta number of their tumors by the delta scanner. In order to suppress intestinal and respiratory movements which interfere in obtaining a clear-cut CT scan image, medication with a purgative, enema or cholinergic blocking agent was given or the abdomen was immobilized with special rubber prior to scanning.

With the intention of discriminating the affected organ from those adjacent to it, e.g. the bladder and intestine, the contrast medium was injected into or applied to the bladder, vaginal fornix, etc. as indicated.

2) Tumors extracted were also measured for the delta number.

II. Study of contrast enhancement by Urografin

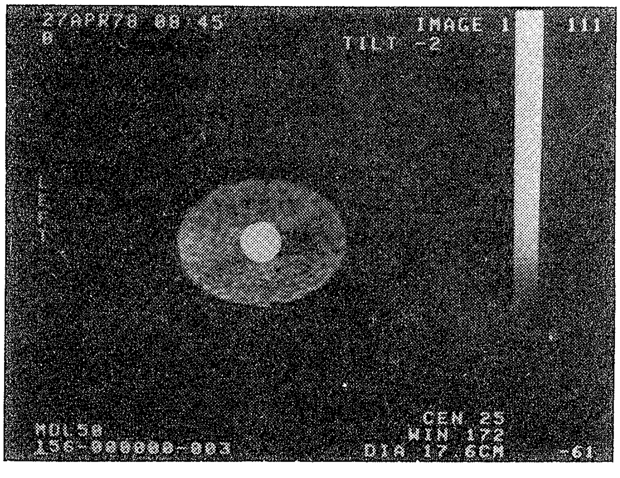
1) Relation between the delta number and iodine concentration.

Serial dilutions (0.5-3.0%) of 60% Urografin (Iodine concentration: 292 mg/ml), each contained in a plastic vessel, 10 mm in inner diameter, were scanned in distilled water. The delta number then was determined as the mean value of a matrix of 60 attenuation coefficient numbers printed out on computer paper (Fig. 1).

2) Methods for introduction of 60% Urografin and changes in the concentration of iodine in the blood.

In order to determine a method of Urografin administration producing the highest enhancement effect in CT diagnosis, two methods for introducing contrast medium, i.e.,

Fig. 1. The mean value of 60 matrixes of the attenuation from the printouts.



12	11	6	12	6	3	13	5	9	10	12	2
4	9	13	3	-3	3	-1	0	-1	7	9	10
7	12	0	-12	-7	-3	3	-4	-3	-3	5	11
3	-13	0	9	14	23	22	23	15	5	-8	0
-5	-4	4	30	37	34	38	27	25	25	5	1
-2	0	26	37	31	32	34	40	37	25	19	4
-6	17	29	30	35	28	34	32	29	31	31	14
-7	10	31	39	26	34	31	36	36	30	35	7
-4	17	27	34	38	36	33	33	27	31	31	16
-7	8	35	39	28	34	35	33	35	39	26	14
-7	12	24	30	34	35	30	[illegible]	32	33	28	[illegible]
-4	-15	19	33	32	[illegible]	40	33	30	[illegible]	17	4
-6	-13	-12	10	15	[illegible]	35	28	25	4	-1	-3
[illegible]	-6	-4	0	6	3	13	10	-10	-3	-1	4
4	[illegible]	5	-10	-7	-1	-4	-6	-3	[illegible]	0	10
4	7	4	11	[illegible]	1	1	5	0	[illegible]	17	7
[illegible]	17	11	5	6	5	14	4	[illegible]	20	9	7

bolus injection* and biphasic infusion**, were examined for their adequacy for diagnostic purposes.

*bolus injection: 100 ml of Urografin is rapidly injected intravenously before the scan is made.

**biphasic infusion: 50 ml of Urografin is rapidly injected intravenously prior to the start of scanning and subsequently another 50 ml of the contrast medium is administered by intravenous drip infusion at a rate of 50 ml/10 min. ("biphasic-10") or 50 ml/20 min. ("biphasic-20") during which time repeat scans are made.

From patients and healthy individuals receiving Urografin either by bolus injection or by biphasic infusion ("biphasic-10", "biphasic-20") heparinized blood samples were taken before, and 5 to 60 minutes after the administration of the iodinated contrast medium for estimation of the iodine concentration in blood. The blood specimens were also measured for the delta number by the method described in 1) above to investigate the time course of its changes.

III. Changes in the delta number of tumors following the injection of Urografin

Determination was first made of the delta number of cross-sections of ovarian tumors and uterine myomas in view of the fact that these tumors are best visualized on such slices by plain scan (pre-contrast scan). Then 60% Urografin was injected by the method of "biphasic-20"; 5, 10, 20 and 30 minutes thereafter scans were made of the same cross-sections at the same places (post-contrast scan) for measurement of the delta number.

The attenuation enhancement ratio (A.E.R.) defined as the ratio of the delta number of a post-contrast scan to that of a pre-contrast scan was thus estimated for ovarian tumor, uterine myoma and other lower abdominal tumors for comparison.

Results

1) The delta numbers of varying dilutions of Urografin in distilled water were as indicated in Table 1 and Fig. 2. There was a linear relationship between the concentration of iodine and the delta number, a dilution of the contrast medium containing 100 mg/dl of iodine showing a delta number of 32.5.

2) Changes with time of the concentration in blood of iodine following the injection of 60% Urografin by the different methods stated above are represented in Fig. 3.

Following bolus injection the blood level of iodine was steeply elevated to a peak and then rapidly declined, the percentage decrease from the peak level being 12.5% at 5 minutes, 18.8% at 10 minutes and 28.5% at 30 minutes.

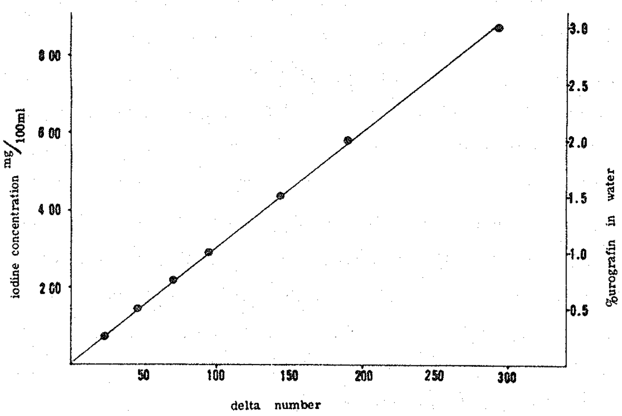
With the contrast medium injection by "biphasic-10" (50 ml bolus injection + 50 ml drip infusion in 10 min.) the blood level of iodine peaked 10 minutes after starting the injection and thereafter was lowered by 10.9%

Table 1. Attenuation values of different dilutions of 60% urografin in distilled water

Iodine concentration mg/dl of mixture	Attenuation value
73	23.4
146	46.7
219	70.1
292	94.9
438	143.7
584	189.3
876	293.0

100 mg/dl iodine — 32.5 delta scale unit

Fig. 2. The relationship between the delta number and iodine concentration.



at 20 minutes and by 16.5% at 30 minutes.

Urografin injection by "biphasic-20" (50 ml bolus injection + 50 ml drip infusion in 20 min). yielded a similar pattern of changes in the blood level of iodine to that observed with "biphasic-10" for the initial 10 minutes. For ensuing periods, however, the concentration of iodine in the blood was maintained at a higher level than with "biphasic-10".

3) The time course of the delta number of solid ovarian tumor and uterine myoma following the contrast medium injection by "biphasic-20" is given in Fig. 4.

The bolus injection of 50 ml Urografin was followed by a gradual increase in contrast for both types of tumor. Five minutes after the bolus injection the curves almost attained a plateau and began to decline at 20 minutes (end of drip infusion).

4) Table 2 indicates the delta number of various gynecologic tumors of proven histopathology as calculated from pre-contrast scans. As can be seen, the ranges of value of the delta number found were 40-55 for uterine myoma, 35-45 for carcinoma corporis uteri, 40-50 for missed abortion, 8-22 for hydatidiform mole and 20-35 for chorio carcinoma.

Cystic ovarian tumors, except for dermoid cyst, gave a delta number of 0-40. More particularly, serous cystoma showed a value of 0-18, mucinous cystoma 15-25 and tarry cyst 25-40. Dermoid cyst gave the followng attenuation values: fat −150∼−130, teeth & bone 400-900, hair-containing portion −90∼−70.

Solid ovarian tumor, on the other hand, showed a relatively high delta number of 32-70. A comparison of the delta number of cystic vs. solid ovarian tumor is given in Fig. 5. As is obvious from the figure, these two types of ovarian tumor could be differentiated from each other in terms of the difference in precontrast delta number in most instances. However, where the delta number was within the range of 30 to 40, no distinction could be made between the two types of tumor by this radiodiagnostic procedure.

Fig. 3. The change of the iodine concentration in blood.

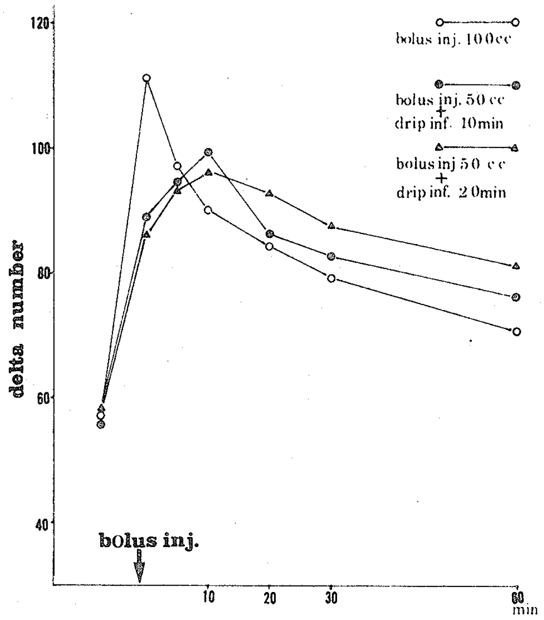
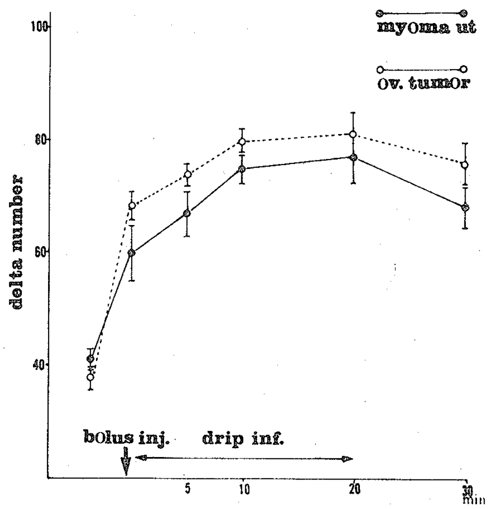


Fig. 4. The change of the delta number in enhanced tumors.



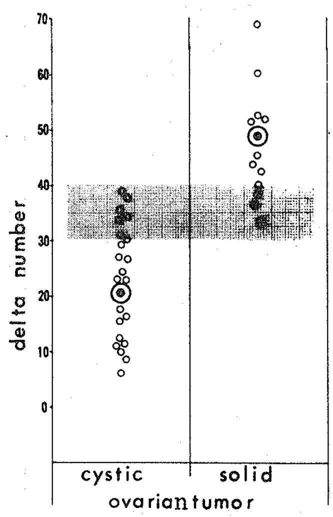
Extracted tumors also were measured for the delta number, but the values found were essentially the same as those for normal tissues.

5) Table 3 gives values of the attenuation enhancement ratio (A.E.R.) for various tumor types. As is apparent from the table, the value was 1.0 (no change) for cystic ovarian tumors, 2.04±0.2 for solid ovarian tumor, 1.75±0.2 for intramural or submucosal uterine myoma and

Table 2. Delta number of gynecological tumors

	Cases	Delta number	
cystic ovarian tumor			
serous cystoma	10	0~18	
mucinous cystoma	7	15~25	
dermoid cyst	5	400~900 −150~−130	bone, teeth fat
tarry cyst	6	25~40	
solid ovarian tumor	14	32~70	
myoma uteri	22	40~55	
carcinoma corporis uteri	3	35~45	
missed abortion	3	40~50 40~55	endometrial cavity myometrium
hydatidiform mole	4	8~22 34~38	endometrial cavity bleeding lesion
choriocarcinoma	6	20~35	focus in myometrium

Fig. 5. The delta number of Ov. tumors.



1.25±0.2 for polypoid uterine myoma.

In missed abortion, on the other hand, the A.E.R. of the endometrial cavity was 1.11±0.1, hence there was little contrast enhancement. However, a high selective enhancement of the myometrium on post-contrast scan made it possible to distinguish the affected area from the rest of uterine tissues.

Choriocarcinoma was associated with an exceedingly high value for A.E.R. of 3.52±0.2.

In hydatidiform mole, no noticeable contrast enhancement was observed in the tumorous portion, whereas iodine was detected in an unusually high concentration in the area of the bleeding lesion. Fig. 6 gives comparison of pre- and post-contrast delta numbers of various lower abdominal tumors.

Discussion and Conclusion

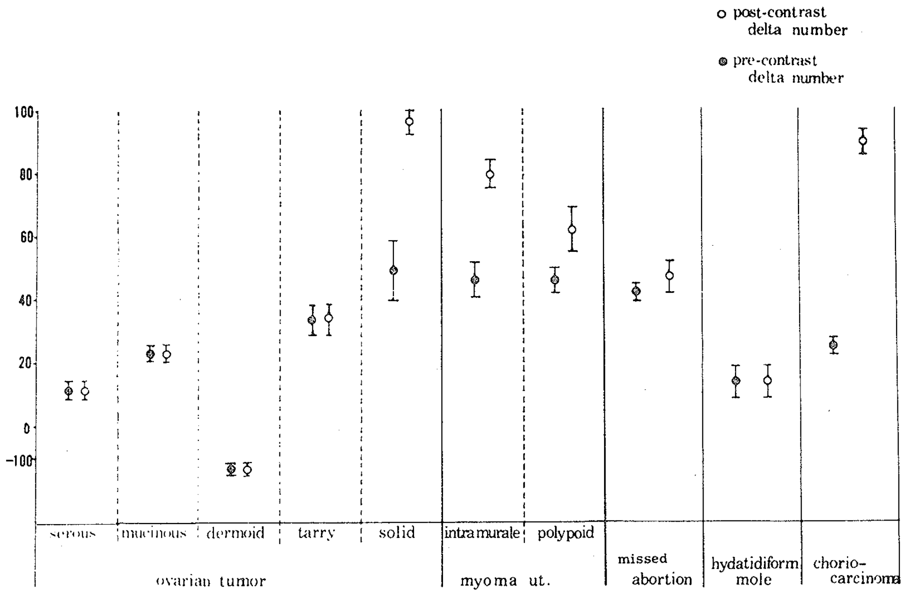
Diagnostic procedures for gynecologic and obstetric diseases have made remarkable progress in recent years. In the diagnosis of gynecological tumors a variety of auxiliary diagnostic tools, such as radiologic procedures (HSG and PAG), endoscopy (culdoscopy and laparoscopy) and aspiration smear, have been used as adjuncts to routine pelvic examination in an effort to enhance diagnostic accuracy. This is because a full understanding of the nature and morphology of tumor prior to operation is of pivotal clinical importance.

Particularly in ovarian tumors, it is virtually impossible to establish diagnosis before the growth of tumor or its metastatic invasion gives rise to specific symptoms. Moreover, not a few of those patients who visit a gynecological

Table 3. Attenuation enhancement ratio (A.E.R.)

	pre-contrast delta num.	post-contrast delta num.	A.E.R.
cystic ov. tumor			
serous	11±2.3		
mucinous	23±4.6	no change	
dermoid	−139±6.3		
tarry	34±4.5		
solid ov. tumor	48±9.5	96±7.8	2.04±0.2
myoma uteri			
intramurales	46±5.7	79±3.6	1.75±0.2
polypoid	50±3.7	62±9.0	1.25±0.2
missed abortion	42±2.5	47±5.0	1.11−0.1
hydatidiform mole	15±5.1	no change	
choriocarcinoma	26±2.6	90±3.5	3.52±0.5

Fig. 6. Comparison of the pre- and postcontrast delta number in the lower abdominal lesion.



service to seek help for such symptoms fail to undergo thorough pelvic examination because of obesity, adhesions or ascites. In such an instances it usually takes a long time for the physician to obtain definite diagnostic evidence.

Apart from special rare cases, it is quite difficult to determine in what organ the tumor in question has its origin and whether it is benign or malignant and also to differentiate the affected organ from the adjacent ones. In order to overcome these difficulties and thereby to help make a correct preoperative diagnosis, a number of supplementary diagnostic means have been devised. However, none of them has proven to be satisfactory and, moreover, many are shown to be distressing and even hazardous to the patient. Thus, a definite diagnosis has been made only upon exploratory laparotomy or surgery in many instances.

Ultrasonic tomography[11,15] and computerized tomography (CT) are a recent valuable addition to the diagnostic armamentarium. In the initial stages the use of CT was limited to the diagnosis of intracranial lesions, but lately technical progress has led to the advent of whole-body CT[1,9,16,17] which is applicable also to the diagnosis of diseases of the thoracic and abdominal organs. Being capable of delineating organs in slices, CT affords fairly accurate information about existing lesions. This radiologic procedure, when supplemented with various adjunctive means, permits demarcation of the organ of interest from the surrounding structures[5], informs the physician of the size of the tumor and its adhesion to adjacent structures, if present, and thus suggests the best possible approach to be chosen at surgery and may thereby prove of salient diagnostic use. Being less time-consuming than any other diagnostic means available heretofore and because of the high reliability of information it provides, outstanding are the features of this diagnostic technique.

In the present study, determination was first made of the X-ray attenuation of various lower abdominal tumors in terms of the delta number from their preoperative CT scans in an attempt to estimate the physical properties of the tumors. Then, the preoperative information was collated with intraoperative findings as well as with the diagnosis established postoperatively. In fact, preoperative CT diagnoses were highly consistent with postoperative diagnoses.

It seems that the preoperative CT diagnosis, in many instances, is sufficiently reliable for selecting the procedure and approach for the coming operation. It should be mentioned, however, that there was no substantial difference between the serous and mucinous types of cystic ovarian tumor in delta number and also that distinction could hardly be made between cystic ovarian tumors (notably tarry cyst) and solid ovarian tumors by CT scan when the delta numbers of these two types of tumor were in the range of 30 to 40 (Fig. 5).

In occasional cases uterine myoma and solid ovarian tumor could not be differentiated from each other by this procedure.

Research efforts to further increase the differential diagnostic accuracy of CT scan have led to the availability of the contrast enhancement method which entails the injection of an appropriate contrast medium[2,6,10].

The first step within the framework of this study was to investigate the fundamental aspects of the contrast enhancement method using 60% Urografin as the test agent.

The results agreed well with a report of Godo et al.[8], indicating that a linear relationship exists between the iodine concentration of Urografin and the delta number, and in fact, an iodine concentration of 100 mg/dl corresponds to a delta number of 32.5 (Table 1, Fig. 2).

Two methods, i.e., bolus injection and biphasic infusion, are in use for the intravenous administration of contrast media. The present study showed that "biphasic-20" (Urografin 50 ml i.v. + 50 ml drip infusion in 20 min.) yields constant blood levels of the contrast medium and is best suited to radiodiagnostic purposes.

This finding seems to correspond to a report of Takeda et al.[13] on 65% Angiografin. As reported previously by Cattel et al.[3], the bolus injection of Urografin was followed by a rapid decline of the iodine concentration in the blood.

Norman and his associates[4] found in brain surgery that the administration of an iodinated contrast medium by biphasic infusion was associated with rather low blood levels of iodine and a delayed appearance of maximum contrast enhancement. They stated that the bolus injection of a maximum safe dose is to be preferred. In any event, one should choose the method of contrast medium injection which is considered most appropriate under existing circumstances, taking into account the location of the tumor and the time span required for execution of a scan.

In the present study the author employed "biphasic-20", a method of contrast medium injection known to ensure longsustained blood levels of iodine, in the CT scan of various lower abdominal tumors, and succeeded in differentiating between 2 types of tumor (which gave overlapping delta numbers on precontrast scan), e.g. solid and cystic ovarian tumors, by a discrepancy in the magnitude of difference between pre- and postcontrast delta numbers. The difference in contrast enhancement by a contrast agent is assumed to come from differences in the vascularity of and the amount of extravasated fluids in the tumor and a resultant difference in the concentration of the contrast agent[8].

Choriocarcinoma, solid ovarian tumor and uterine myoma demonstrated a marked contrast enhancement, their A.E.R. (ratio of post- to precontrast delta number) being 3.52, 2.04 and 1.75, respectively. Contrast enhancement was particularly marked with choriocarcinoma, which suggests its possible usefulness in the differential diagnosis of this tumor.

On the contrary, no noticeable contrast enhancement was observed with ovarian cyst, hydatidiform mole or missed abortion.

Surgical evacuation of the uterus as a means of diagnosing choriocarcinoma is quite dangerous and contraindicated. Differentiation between choriocarcinoma and missed abortion reportedly was not satisfactorily made by precontrast scan[14]. The use of the contrast enhancement method has rendered it possible to make both a differential diagnosis of the two diseases and a separate diagnosis of individual conditions.

Investigations of various contrast media are now underway in an effort to achieve satisfactory contrast enhancement in CT scan. According to Messina et al.[7], contrast enhancement was not attained to any appreciable extent in cystic tumors, although their report is based on practice in other fields of medical science than ours.

The results of our present study seem to permit us to assume that so far as the CT scan study of gynecological tumors is concerned, it is possible to obtain an adequate contrast enhancement, and hence correct estimates of the delta number, by injecting the contrast medium by "biphasic-20" (Urografin 50 ml i.v. + 50 ml drip infusion in 20 min.) and then starting the scan 5 minutes later.

In making a CT scan one should always keep the risk of exposure to more than the permissible quantity of X-ray in mind. In view of a report by Tada et al.[12] stating that 7 successive scans incurred an exposure to X-ray in a total quantity of 3-5 rem in a patient, a scan should be made no more than twice for the diagnosis of ovarian tumors in juvenile patients.

Acknowledgement

The author wishes to express his sincere gratitude to Prof. T. Fukushima for his kind instruction and supervision. The wholehearted cooperation of Drs. G. Hoshi and S. Kwak (General Aizu Central Hospital) during this work is also gratefully acknowledged.

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(Accepted: No. 4474, January 12, 1979)

概要 1) 目的：全身用 CT による婦人科腫瘍診断は，無侵襲で診断適中率が高く，臨床上きわめて有用であるが，更に診断精度を増すため確実性のたかい鑑別方法を検討した．

2) 方法：婦人科疾患78例を対象に Delta-scanner 50 による診断を行つた．i) 各種婦人科腫瘍の in vivo 及び剔出後の in vivo における density を比較検討した．ii) 60% Urografin を用い，ヨード濃度と CT 常数とを比較検討，ついで bolus inj., biphasic inf. (10分間，20分間) によるヨード血中濃度の時間的変化を調べた．iii) biphasic inf. (20分間) により充実性卵巣腫瘍及び子宮筋腫における同一面内における時間的 enhanced density の変化及び各種腫瘍の Attenuation Enhancement Ratio (A.E.R.) を得た．

3) 成績：i) 各種腫瘍群における density と組織性状とには一定の関連があり，in vivo 及び in vitro においても差異は認めなかつた．またある腫瘍においては density に overlapping range がみられ，鑑別が困難であつた．ii) ヨード濃度 CT 常数とは直線関係にあり，iodine 100mg/dl=32.5, delta scale unit であつた．iii) スキャン中に血中濃度を一定にするには，biphasic inf. 法がすぐれていた．iv) 腫瘍内の enhanced density の変化は10—20分後に peak となり，静注後5分以上経過してスキャンを開始する必要がある．v) A.E.R. は絨毛上皮腫 (3.52±0.2) 充実性卵巣腫瘍 (2.04±0.2) 子宮筋腫 (1.75±0.2) で著明な contrast enhancement (CE) が得られた．これに反し，嚢腫壊死部分では CE は認めがたかつた．vi) CT 診断にて density の overlapping により鑑別不可能であつた症例も，CE を応用することにより鑑別を容易にした．