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Dynamic hepatic CT: uniphasic and biphasic contrast medium injection protocols

Dynamiczna tomografia komputerowa wątroby: jednofazowe i dwufazowe protokoły infekcji środka cieniującego

With the advent of faster computed tomographic (CT) scanners, there has been a renewed interest in evaluating techniques of intravenous administration of contrast material for enhancement of liver parenchyma with abdominal CT. There is an extreme controversy as to the proper method of administration of contrast material to document metastatic liver disease, prime tumors of liver and even over assessing contrast material enhancement of normal liver. Although the use of intravenous contrast material is generally agreed to increase the conspicuity of focal hepatic lesions and the sensitivity of CT in their detection, less agreement exists regarding the method by which contrast material should be administered. Numerous investigators compared the effect of biphasic (double flow rate) and uniphasic (single flow rate) injection techniques with various contrast material volume (2, 3, 8, 10, 12, 13, 15). Also the optimal rate of contrast material injection and the delay between the start of the bolus and beginning of scanning remain matters of controversy (1, 4, 6, 7, 11). Another major point is to define the optimal injection protocol providing better enhancement for detection of liver masses (1, 5, 9).

The purpose of this study was to compare hepatic contrast enhancement attained by using uniphasic and biphasic injection protocols with both high and low flow rates.

MATERIAL AND METHODS

One hundred eleven patients referred for CT scanning of the abdomen were randomized into nine groups with different intravenous contrast medium injection protocols (Tab. 1). The patient population consisted of 46 women and 65 men (mean age of the patient 47 years); their median weights 69 kg. Patients specifically excluded from the study were those with diffuse hepatic parenchymal disease, a serum creatinine level higher than 220 μmol/L, diastolic blond pressure higher than 120 mmHg, congestive heart failure, or a contraindication to receiving iodinated contrast material.

All CT scanning was performed with a Somatom DRH scanner (Siemens) by using a 2–second scanning time and a 6–second interscanning delay. Contiguous 8 mm sections were obtained, begin-

Table 1. Contrast medium injection protocols

N	Bolus	Concentr. I/ml	Volume [ml]			Dose jod (g)	Rate injection (ml/s)		Injection time (s)		
			dose	dose	dose		dose	dose	dose	dose	dose
13	60/2	300	60	60	–	18	2	–	30	30	–
8	60/3	300	60	60	–	18	3	–	20	20	–
7	80/3	300	80	80	–	24	3	–	27	27	–
6	100/2	300	100	100	–	30	2	–	50	50	–
4	100/3	300	100	100	–	30	3	–	34	34	–
35	125/3	300	125	125	–	38	3	–	42	42	–
10	125/5	300	125	125	–	38	5	–	25	25	–
17	125/3/1*	300	125	60	65	38	3	1	85	20	65
11	125/5/2**	300	125	60	65	38	5	2	45	12	33

* hipsasic flow biphasic flow, ** hipsasic flow biphasic high

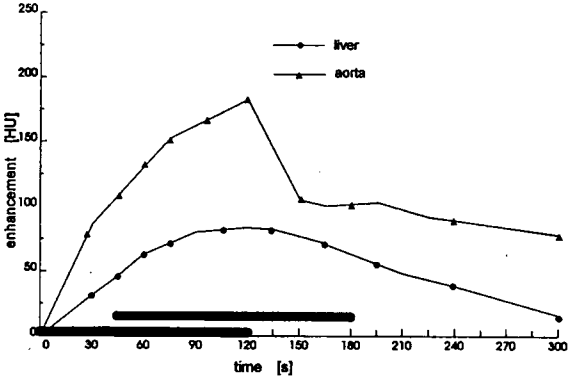

Fig. 1. Determination of the onset of the equilibrium phase (model proposed by Foley)

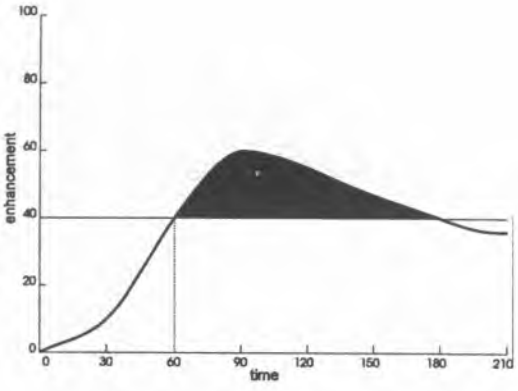

Fig. 2. Contrast enhancement index
(model proposed by Heiken)

ning at the diaphragm. Scanning began 30–40 seconds after the start of administration of the intravenous contrast material bolus. Each patient received a different dose of contrast medium up to 125 ml of 60% uropolina.

Attenuation values of the liver and aorta were measured from a single precontrast scan obtained at the level of the main portal vein, by using a circular region of interest (ROI – 2 cm^2) cursor. Attenuation values of liver and aorta were then obtained from scans obtained at 30, 39, 48, 57, 66, 75, 84, 93, 102, 11 l, 140, 170, 200 seconds after the start of the contrast medium bolus.

In the liver, ROI_S were measured in three separate areas including both left and right lobes, and the results were average. Vessels were carefully excluded from the ROI measurements. Enhancement parameters calculated for each patient included maximum liver enhancement, the time from the start of the contrast medium bolus to maximum liver enhancement, the time from the start of the bolus to various levels of liver enhancement (10, 20, 30, 40, 50 and 60 HU) and the time from the start of the bolus to onset of the equilibrium phase.

To determine the onset of the equilibrium phase, a theoretical model proposed by Foley (8) was used. According to this model, the equilibrium phase occurs when the aortic and hepatic contrast enhancement curves become parallel and begin to decline at a similar rate (Fig. 1) and during which a substantial part of the hepatic enhancement is due to contrast material in the extravascular space. Other enhancement parameters were measured: maximum aorta enhancement, the time from the start of contrast medium bolus to maximum aorta enhancement, the time from the start of the bolus to various levels of aorta enhancement (10, 20, 30, 40, 50, 60 HU), the time from the start of the bolus to a desired level (threshold) of liver enhancement, the optimal scanning interval (LSI liver scanning interval), contrast enhancement index (CEI) as the area under the hepatic contrast enhancement curve Fig. 2).

When the overall differences were statistically significant, analyses were performed by using statistics for Windows, Math Cad programs and t–student test and ANOVA test.

RESULTS

The time to maximum liver enhancement for among the nine protocol groups were demonstrated (Tab. 2). The injection protocols with hight flow rates (5 ml/sek.) showed that peak hepatic enhancement is reached sooner when more rapid injection rates are used (for 125/5 ml/s – time to peak 47.6 sec. For example, bolus with biphasic low flow 125/3/1 ml/sec. time to peak 93.8 sec.

Table 2. Time to maximum liver enhancement

N	Bolus	Time injection (s)	Time to maximum liver enhancement (s)	Time to peak enhancement after time injection (s)
13	60/2 ml/s	30	50.92 ± 14.71	20
8	60/3 ml/s	20	43.37 ± 17.37	23
7	80/3 ml/s	27	56 ±16.05	29
6	100/2 ml/s	50	54.5 ± 12.47	5
4	100/3 ml/s	33	62.25 ± 15.19	28
35	125/3 ml/s	42	67.22 ± 14.77	9
10	125/5 ml/s	25	47.6 ± 3.7	22
17	125/3 ml/s	85	93.82 ± 26.48	9
11	125/5 ml/s	45	80.73 ± 6.08	35

Peak hepatic enhancement increases with increased volume of contrast material or rate of injection (Tab. 3) (Fig. 3). Among all injection protocols the highest maximum hepatic enhancement was by means uniphasic bolus contrast medium 125 ml/5ml/s. Uniphasic injection was superior to biphasic injection for maximum hepatic enhancement (74 ± HU and 52 ± 6 HU). Also uniphasic injection was superior to biphasic injection for maximum enhancement of aorta (244 ± 95 HU and 136 ± 34 HU) (Tab. 3).

The injection protocols with hight flow rates (5 ml/sec.) provided greater maximum aorta and liver enhancement than did the protocols with lower flow rates (3 ml/sec.). Only the difference between the uniphasic high flow rate and biphasic low flow rate protocols, however, was statistically significant (Tab.3).

The time to enhancement threshold and equilibrium from the start of the bolus to maximum liver enhancement for the nine protocol groups is listed in (Tab. 4) The time intervals from the start of the bolus to the onset of equilibrium phase were significantly greater for biphasic protocols than for the uniphasic protocols (216 ± 44 s and 81 ± 14 sec.).

Table 3. Maximum aorta and liver enhancement

N	Bolus	Maximum aorta enhancement (HU)	Maximum liver enhancement (HU)
13	60/2 ml/s	169.44 ± 41.1 [a,b]	34.36 ± 9.47 [a]
8	60/3 ml/s	185.4 ± 79.01 [a,b]	32.21 ± 11.44 [a]
7	80/3 ml/s	167.17 ± 54.38 [a,b,c]	38.71 ± 7.38 [a]
6	100/2 ml/s	196.12 ± 9.38 [a,b,c]	52.06 ± 12.89 [c,d]
4	100/3 ml/s	202.65 ± 54.91 [b,c]	62.52 ± 6.7 [b,d,c]
35	125/3 ml/s	196.44 ± 41.1 [b,c]	60.34 ± 13.6 [b,d]
10	125/5 ml/s	244.07 ± 95.09 [b]	74.21 ± 10.37 [e]
17	125/3/1 ml/s	136.4 ± 34.23 [a]	52.36 ± 6.1 [c]
11	125/5/2 ml/s	179.73 ± 29.79 [c]	64.46 ± 9.04 [b]

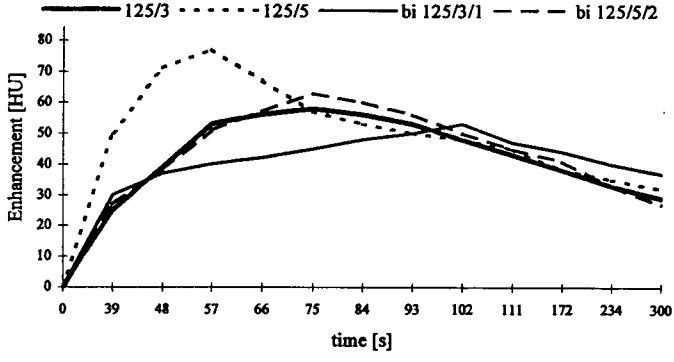

Fig. 3. Contrast enhancement curves for various different bolus of contrast medium

The optimal scanning interval, defined as the length of time between the onset of a desired level of hepatic enhancement and either the decline of enhancement below the desired level or the onset of the equilibrium phase was evaluated for hepatic enhancement levels of 10–60 HU for each protocol. The optimal scanning interval for biphasic protocols was significantly longer than for the uniphasic protocols at every level of hepatic enhancement.

The CEIs for the biphasic protocols were significantly higher than for the uniphasic protocols at 10, 20, 30, 40 UH of hepatic enhancement (Fig. 4). At 70% of hepatic enhancement, the CEI for

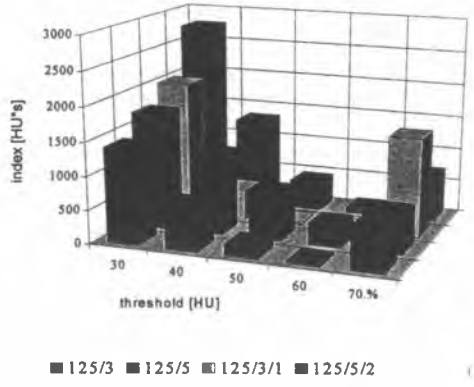

Fig. 4. Contrast enhancement index for different enhancement thresholds

Table 4. Time to enhancement threshold (s) and equilibrium

N	Bolus	Time to threshold enhancement (s)	Time to onset equilibrium (s)
13	60/2 ml/s	31.61 ± 10.67 [a]	71.92 ± 16.46 [a,b]
8	60/3 ml/s	31.35 ± 11.9 [a]	64.5 ± 19.59 [a]
7	80/3 ml/s	40.71 ± 10.32 [a,b,d]	105 ± 44.24 [c,d]
6	100/2 ml/s	39.33 ± 9.02 [a,b]	101.28 ± 27.51 [b,c,d]
4	100/3 ml/s	43.25 ± 9.17 [a,b,d]	107.15 ± 5.09 [c,d]
35	125/3 ml/s	44.51 ± 9.92 [b,d]	127.45 ± 37.46 [d,f]
10	125/5 ml/s	29.5 ± 6.65 [a]	81 ± 14.77 [a,b,c]
17	125/3/1 ml/s	51.176 ± 15.6 [c,d]	216.17 ± 44.1 e
11	125/5/2 ml/s	49.9 ± 9.21 [d]	140.3 ± 19.04 [f]

biphasic low rater protocols was significantly higher than for other three protocols. Optimal time windows for uniphasic and biphasic bolus injection are shown in Figures 5, 6.

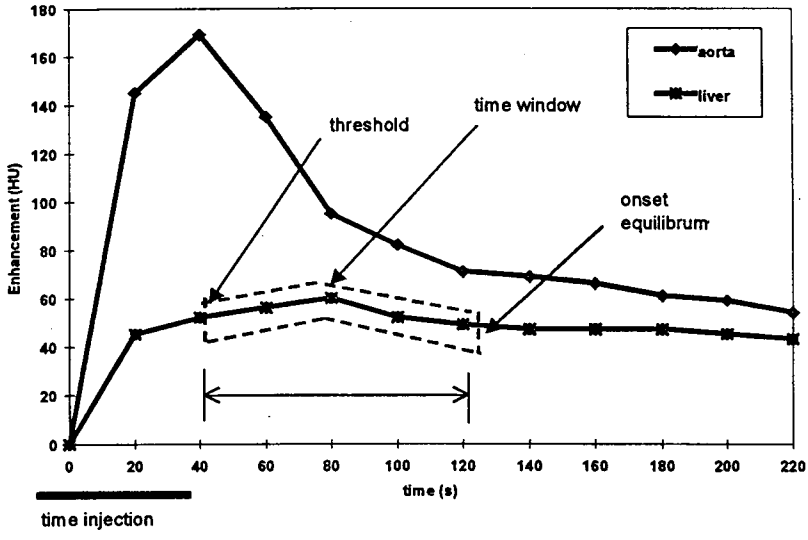

Fig. 5. Optimal time window for uniphasic bolus injection
(125 ml/3 ml/s)

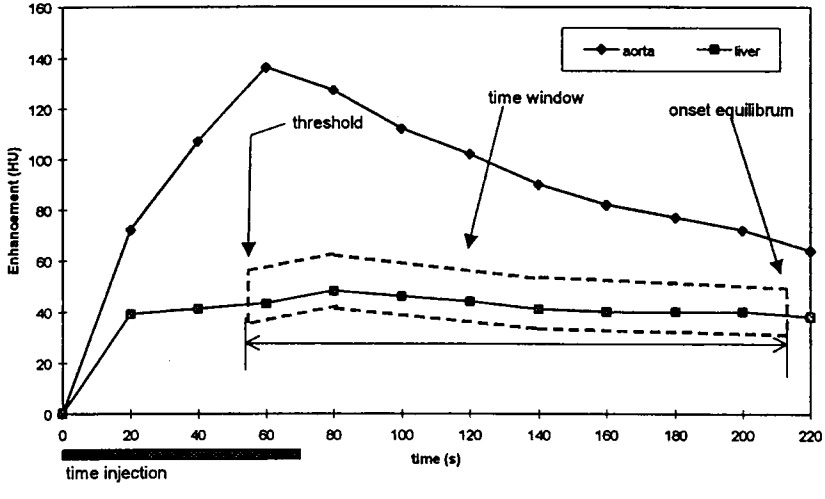

Fig. 6. Optimal time window for biphasic low bolus injection
(125 ml/3 ml/s/1 m/s)

DISCUSSION

For the detection of focal hepatic lesions, the goal of intravenous contrast medium administration is to widen the difference in attenuation values between tumor and normal hepatic parenchyma. Several studies have shown the peak hepatic enhancement increases with increased volume of contrast material or rate of injection (l, 3, 4, 6, 7, 8, 10, 11).

Although it is generally agreed that intravenous administration of contrast material is necessary to image hepatic lesion and that bolus infusion is preferable to drip infusion, a consensus is lacking about the optimal injection protocol. Some researchers advocate uniphasic and others prefer biphasic injection protocols. One prominent theory asserts that optimal detection of lesion depends on completion of liver scanning before "equilibrium". Many authors exhibit that most liver hypervascular lesions include some examples of hepatocellular (hepatoma) renal cell, thyroid, carcinoid, melanoma, some forms of sarcoma, and other less common lesions that should be examined before equilibrium phase (1, 3, 8, 10, 15). These metastases are detected better in the arterial phase and are usually obscured in the portal phase. On the other hand, hypovascular metastases which represent the majority of liver metastases are detected better in the portal phase (1, 5, 9, 10).

Consequently, detection of very small metastases (smaller than 1 cm) would be a real challenge for most of currently used imaging modalities. With the old technology of incremental CT, the whole liver is imaged in 2–5 min., too long a time to pick up the arterial phase except perhaps in the first acquired slices. With the advent of the new technology of spiral CT and electron–beam CT, it has become possible to examine the whole liver in 20–30 s. This allows repeated imaging of the whole liver in the arterial phase and in the portal phase (3, 11, 14).

Dynamic incremental CT is still the most widely available and the preferred routine technique for detecting liver lesions, and several studies have reported improvement of lesion–to–liver contrast with CT scans performed within 2–3 min. after administering a bolus of contrast medium. The purpose of this article was to understand and optimize the use of contrast material for dynamic CT of the liver.

Our studies have shown that peak hepatic enhancement increases with increased volume of contrast material and rate of injection. In addition, peak aorta and hepatic enhancement were reached sooner when more rapid injection rates were used.

Our results show that in each group, the faster rates of injection resulted in the shorter time to peak aorta and liver enhancement. When a faster rate of injection was used, peak liver and aorta enhancement occurred earlier. In our study, when the two rates of injection were compared by time intervals, mean liver enhancement increased significantly with the faster rate of injection but only during the earliest time intervals (57–75 seconds). For biphasic injection mean liver enhancement increased during the later time interval 75–100 seconds (Fig. 3). Small et al. also showed that early liver enhancement increased with an injection rate of 5 ml/s compared with 3 and 4 ml/s rates (14).

Our results show that the uniphasic injection was superior to the biphasic injection for all combinations of concentration and volume tested in this study. This differs from our study of injection techniques during conventional scanning in which we found that a biphasic injection with a high initial flow rate was superior to uniphasic injection because it delayed the onset of equilibrium and provided a longer optimal scanning interval. These results are similar to a study performed by Heiken et al. and by Foley et al. (8, 10). Berland and Lee also found the rapid uniphasic injection of contrast material superior to the prolonged biphasic injection for conventional dynamic CT (4). The precise point at which the equilibrium phase begins is difficult to determine. When the distribution of

intravascular and extravascular contrast material equilibrates, the iodine concentration declines slowly at a rate determined by renal filtration. Foley (8) has proposed that the onset of the equilibrium phase occurs at the point when the aortic and hepatic contrast enhancement curves become parallel and decline at an equal rate (Fig. 1). We used this model to determine the effect of different injection protocols on the onset of the equilibrium phase. Our data indicate that the onset of the equilibrium phase is delayed with biphasic injection, in comparison to the onset after uniphasic injection. With the biphasic protocols, the mean onset of equilibrium phase was 140.3–216.17 seconds for 125/5/2 ml/s. and 125/3/ 1 ml/s. after the start of the contrast medium bolus, compared to 87–127 seconds for 125/5 ml/s. and 125/3 ml/s. with the uniphasic protocol. In our study, the optimal scanning interval for biphasic protocol was longer than for the uniphasic protocols at every level of desired hepatic enhancement (10–60 HU) because of the delay in onset of equilibrium phase (Tab. 4). For hepatic enhancement thresholds of 40 HU, or greater, the biphasic protocol provided longer optimal scanning intervals than did the uniphasic protocol. The level of peak hepatic enhancement and the length of the optimal scanning interval are important factors to determine the optimal technique for liver contrast enhancement. The CEIS for the biphasic protocols were significantly higher than for uniphasic protocols at all desired levels of hepatic enhancement (Fig. 4).

The ability of CT contrast technique to show hepatic tumors is enhanced by the dual blood supply of the liver. The liver is different from all other abdominal organs because of its dual blood supply. The hepatic artery delivers 20–25% of blood flow to liver, and the portal vein delivers 75–80% (1). This and the fact that most tumors of the liver have only a hepatic arterial blood supply and receive little or no flow from the portal vein are the key physiological parameters that make contrast–enhanced CT so successful in detecting tumors (1, 8). Compared with slow and prolonged rates of contrast administration or enhancement CT, dynamic incremental bolus contrast–enhanced CT has been found to be the most sensitive method of contrast administration for detecting hepatic neoplasms. This technique requires the use of a power injector to ensure a rapid and sustained rate of infusion of contrast material and to avoid scanning during the equilibrium phase of contrast enhancement. In our study the longest time to window "scanning window" determined as the time between threshold enhancement and onset equilibrium showed biphasic low flow rate bolus (Fig. 5, 6).

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STRESZCZENIE

Celem pracy było opracowanie optymalnej techniki d–TK umożliwiającej obrazowanie wątroby w konwencjonalnych skanerach TK z czasem 8–9 skanów/minutę.

Grupę badaną stanowiło 111 chorych, których z różnych wskazań klinicznych kierowano do d–TK nadbrzusza. W szczególności poddano ocenie wpływ różnych dawek środka cieniującego i szybkości bolusa na poziom maksymalnego wzmocnienia kontrastu wątroby, wpływ różnych dawek środka cieniującego i szybkości bolusa na czas do użytecznego diagnostycznie progu wzmocnienia kontrastu, czas pojawiania się fazy równowagi oraz wartość indeksu kontrastowego wzmocnienia wątroby.

Z przeprowadzonych badań wynika, że optymalną techniką d–TK umożliwiającą obrazowanie całej wątroby może być bolus jednofazowy dla warunków badania 125 ml środka cieniującego i szybkości przepływu 3 ml/s – ze względu na korzystne średnie wartości maksymalnego wzmocnienia kontrastu i dostatecznie szeroki przedział czasu obrazowania. Z porównania różnych profilów bolusa dynamicznego wynika, że najbardziej efektywny w obrazowaniu całej wątroby jest bolus dwufazowy wolny (125 ml/3/ 1 ml/s) ze względu na najwyższe wartości indeksu wzmocnienia kontrastowego i szerokie „okno" czasu obrazowania.