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Optimization of automatic bolus tracking for timing of the arterial phase of helical liver CT

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Abstract The aim of this study was to optimize bolus tracking for timing of the arterial phase of biphasic helical liver CT and to compare optimized bolus tracking to a standard delay. One hundred fifty patients were examined with six protocols: 5- or 10-s delay after triggering at a threshold of 50 or 75 or 100 HU enhancement in the aorta at the origin of the celiac arteries after injection of 120 ml contrast material at 3 ml/s. Optimal arterial enhancement was defined as 20–30 % of hepatic enhancement in portal venous phase. Another 50 patients were examined with the optimized protocol and compared to 50 gender- and age-matched patients who underwent a 25-s standard delay. A 10-s delay after the 75-HU threshold resulted in the most patients with an optimal arterial phase ($p < 0.01$). Thirty-one of 75 patients examined with this protocol showed optimal early liver enhancement. Bolus tracking compared with standard delay revealed only a trend for a difference ($p = 0.07$). The outcome of automatic bolus tracking differs depending on the protocol used; however, optimal arterial phase imaging was seen in only 41 % of patients, indicating only a trend for superior timing compared with a standard delay.

Keywords CT · Contrast media · Liver

Introduction

In contrast to all other abdominal organs, the liver has a dual blood supply. Twenty-five percent of blood flow is delivered by the hepatic artery, 75 % by the portal vein [1, 2]. Most tumors of the liver, however, are exclusively supplied by the hepatic artery [3]. This physiological phenomenon allows detection of liver lesions by use of biphasic helical computed tomography (helical CT). Hypervascular lesions can be detected in the arterial phase, whereas hypovascular lesions present in the portal venous phase, respectively [4].

Using a standard delay time before initiation of scanning after the start of contrast administration neglects the varying transit times of the contrast bolus among patients. With automatic bolus tracking, the density of a region of interest (ROI) and, therefore, the contrast enhancement can be measured and biphasic helical CT can be optimized for individual patients [5, 6]. In the literature, mostly a hardware–software upgrade of GE HiSpeed Advantage scanner is used for this purpose (SmartPrep, General Electric, Milwaukee, Wis.) [5, 6, 7, 8, 9]. With a new software, a nearly continuous data acquisition with a reconstruction time of 0.5 s and, therefore, a closer detection of the contrast bolus is possible (CARE Vision, Siemens, Germany). Threshold and delay after triggering now might gain a higher influence on the optimal time point for the initiation of the helical scan. The purpose of this study was twofold. Firstly, we wanted to identify the optimal threshold and start delay after triggering using six protocols for optimal timing of the arterial phase. Secondly, after determination of the optimal protocol, the utility of bolus tracking was tested in a routine clinical setting in comparison with patients examined with an empirical standard delay time for scanning after contrast injection.

Table 1 Groups A–F with varied values for threshold and delay after triggering. The number of patients is presented for each group that showed a percentual liver enhancement in the arterial phase (related to maximum enhancement in the portal venous phase) of < 20, 20–30, and > 30 %

Group	Threshold (HU)	Delay (s)	< 20 % enhancement	20–30 % enhancement	> 30 % enhancement
A	50	5	18	2	5
B	75	5	15	5	5
C	100	5	17	6	2
D	50	10	7	4	14
E	75	10	11	12[a]	2
F	100	10	4	5	16

[a] Significantly more patients ($p = 0.01$)

Materials and methods

All examinations were performed with a helical CT scanner (Somatom Plus 4, Siemens, Erlangen, Germany) using the CARE Vision software version VB30B. The study was approved by our institution's ethics committee, and informed consent was obtained from all patients examined with bolus tracking.

In order to establish a standard delay time, the examinations of 160 consecutive patients (87 men and 73 women; age 51.8 ± 13.5 years; age range 15–76 years), referred to helical CT angiography of the renal arteries, were analysed retrospectively. Ten millilitres of a non-ionic contrast material (Imeron 300, Byk Gulden, Germany) were injected as a test bolus injection into an antecubital vein as used in clinical routine with a flow of 3 ml/s. A helical CT with a pitch of 1.5 and a slice collimation of 2 mm was started 10 s after initiation of contrast injection. The peak transit time from intravenous injection to maximum enhancement of the aorta was determined using a region of interest (ROI) placed in the beginning of the abdominal aorta at the level of the celiac arteries.

Biphasic helical CT of the liver was performed on 150 consecutive patients (81 men and 69 women, age 59 ± 15 years; age range 20–93 years) using automatic bolus triggering. The patient population included inpatients as well as outpatients referred for an abdominal CT examination without selection for suspected liver diseases. Scanning direction was craniocaudal for the arterial phase and caudocranial for the portal venous phase, respectively. Scan techniques included a 0.75-s scan, 120 kV, 200 mAs, pitch 1.5 with a slice collimation of 8 mm. A volume of 120 ml non-ionic contrast material was injected automatically at a flow rate of 3 ml/s using a power injector (Angiomat 6000, Liebel-Flarsheim Company, Cincinnati, Ohio). The ROI for triggering was placed in the abdominal aorta at the level of the celiac arteries. Ten seconds after initiation of contrast administration, a series of nonhelical sequential scans was started. These monitor scans were acquired with a scanning time of 0.5 s (240 ° rotation) in low-dose radiation technique (120 kV, 50 mA) with a cycle time of 1.1 s and a reconstruction time of 0.5 s. The density of the abdominal aorta was measured continuously. For initiation of scanning, threshold and delay after triggering (minimum 5 s, given by the technical equipment) were varied. Patients were randomly divided into six groups A–F with scanning being initiated either with a start delay of 5 or 10 s after triggering at a threshold of 50, 75 and 100 HU enhancement, respectively. All protocols started the portal venous phase with a delay of 60 s after triggering.

For the evaluation of contrast enhancement, ROIs were measured in the abdominal aorta, the portal vein, the right (including cranial, middle, and caudal section) and the left lobe of the liver as well as the spleen; each investigated over approximately the same areas in unenhanced, arterial and portal venous phases. Enhancement of the spleen was evaluated for purpose of comparison with a previous study [9]. Hepatic enhancement in the portal venous phase was defined as maximum density. As a criterion of an optimal arterial phase, a hepatic enhancement of 20–30 % compared with the portal venous phase was defined [5, 10].

After determination of the optimal protocol for automatic bolus tracking, it was applied to an additional 50 consecutive patients (19 men and 31 women; age 59.8 ± 15.4 years). For means of comparison with a standardized start delay after the initiation of the i. v. injection of the contrast material, a control group matched concerning gender and age (19 men and 31 women; age 58.9 ± 14.5 years, 1.3 ± 1.1 years variability) was established and evaluated in the same way. These patients were examined with a fixed delay of 25 and 80 s for the beginning of the arterial phase and of the portal venous phase, respectively, as is usual with our department. This fixed delay time corresponded with a standard delay composed of the mean transit time of the test bolus injected to the patients referred for helical CT of the renal arteries and of the optimal delay after triggering found with groups A–F.

All data are presented as mean ± SD. For statistical analysis a value of $p < 0.05$ was considered to be statistically significant. Kruskal-Wallis test was used for comparison of the six protocols, Wilcoxon matched-pairs test was used for comparison of bolus tracking and standard delay, and Friedman's analysis of variance test was used for the comparison of different liver lobes. Spearman-Rank test was used to study relations between mean transit time or hepatic enhancement and age as well as between enhancement of liver and spleen. Mann-Whitney U-test was used for comparison of the mean transit times at two different ages.

Results

Mean transit time (MTT) in the 160 patients after injection of a test bolus was 15.2 ± 3.3 s, with a minimum of 10 s and a maximum of 30 s. A subdivision of this group by gender showed no significant differences between men and women. There was a significant increase of the peak transit time with age ($r = 0.33$, $p < 0.0001$; Fig. 1), and a subdivision into two groups of age showed a significant difference ($p < 0.001$). Patients < 60 years ($n = 114$) had MTT of 14.6 ± 2.9 s compared to patients ≥60 years ($n = 46$) with MTT of 16.5 ± 3.7 s.

With the 150 patients examined with six protocols, maximum enhancement of the liver was 52 ± 13 HU. Average time from the initiation of contrast injection to crossing of the threshhold was 16.5 ± 4.2 s. Most patients revealing an optimal arterial phase were observed in group E with a delay of 10 s with a threshold of 75 HU ($p = 0.01$; Table 1). There was a moderate correlation between absolute early enhancement of liver and spleen ($p < 0.0001$, $r = 0.48$), with an average enhancement of 13 ± 9 and 51 ± 22 HU for liver and spleen, respectively. In patients with < 5 HU absolute early liver enhancement average spleen enhancement was 32 ± 18 HU.

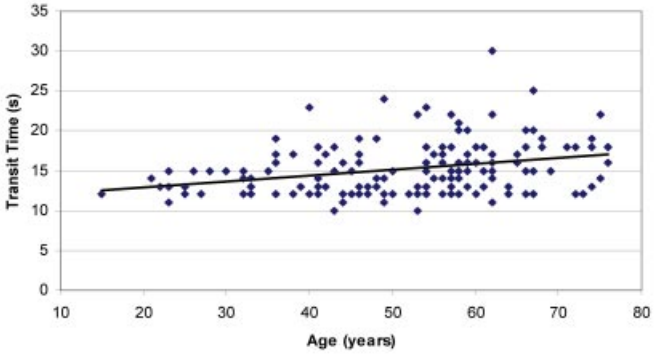

Fig. 1 The relation between age and transit time of 10 ml contrast agent from an antecubital vein to the abdominal aorta in 160 patients. The correlation coefficent is $r = 0.33$ ($p < 0.0001$)

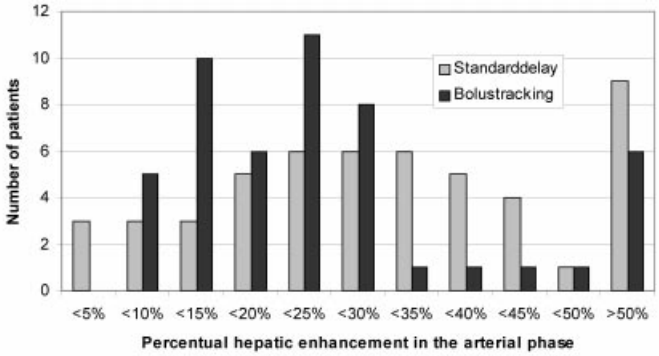

Fig. 2 The percentual liver enhancement in the arterial phase related to maximum enhancement. The *bars* represent the number of patients examined with bolus tracking (group 1) and with a standard delay of 25 s (group 2). There was no significant difference between both groups concerning the number of patients who reached 20–30 % early enhancement

The comparison of 50 additional patients examined with protocol E with the control group of 50 patients with standard delay showed no significant difference concerning the number of patients with an optimal early enhancement (bolus tracking vs standard delay; 19 of 50 patients vs 12 of 50 patients; $p = 0.21$; Fig. 2). Mean early hepatic enhancement as compared with the portal venous phase revealed only a trend for an superior timing over standard delay (bolus tracking vs standard delay; 27 ± 23 vs 33 ± 19 %; $p = 0.07$).

Overall 75 patients were analysed with a bolus timing using the optimal protocol with a threshold of 75 HU and a delay of 10 s. Percentual hepatic enhancement of the arterial phase compared with the portal venous phase was 25 ± 19 % on average. Nevertheless, only 31 of 75 patients had an average hepatic enhancement in the arterial phase between 20 and 30 %. Even a wider definition of an optimal arterial phase (15–35 % enhancement) was met by only 45 of 75 patients. There was a significant decrease of percentual hepatic enhancement with age ($p < 0.01$, $r = –0.35$).

Regarding the overall 53 of 200 patients who presented with optimal average early enhancement of the liver after bolus tracking, the absolute enhancement in the arterial phase was 13 ± 4 HU. Comparing the different ROIs evaluated, a significantly higher percentual enhancement was found in the left lobe (27 ± 10 %) and the caudal section of the right lobe (33 ± 9 %) vs the cranial (18 ± 9 %) and middle (19 ± 6 %) section of the right lobe ($p < 0.0001$). The mean early enhancement of the portal vein was 58 ± 28 HU.

Discussion

In biphasic helical CT, the portal venous phase has a longer predominance, whereas the arterial phase is relatively brief which makes an optimal timing of the arterial phase necessary [10]. In the reviewed literature, fixed delays before initiation of the arterial phase ranged between 20 and 30 s, still with suboptimal contrast enhancement [10, 11, 12, 13, 14, 15]. This is due to the well-known interindividual varying transit times that are described in the literature [16, 17], and that were also found with our patients referred to helical CT angiography of the renal arteries; therefore, there is a need for individual bolus timing that can be performed either by a test bolus injection or by automatic bolus tracking. The latter technique using a new software (SmartPrep) was introduced by Silverman et al. and Kopka et al. [5, 6, 7, 8, 9]. Most studies aimed at the optimization of hepatic enhancement in the portal venous phase with the ROI placed in liver parenchyma [7, 8, 18, 19]. However, automatic bolus tracking can also be used for timing of the arterial phase with the ROI set in the aorta [9, 20].

With our study, the enhancement of the abdominal aorta at the level of the celiac artery was used as an indirect trigger for the arterial phase of the liver. For purposes of optimization, threshold of enhancement and the delay between triggering and the initiation of scanning were varied. A delay of 5 s for initiation of the scan was too short for a liver enhancement of at least 20 %, independent of the trigger values evaluated. Therefore, a delay of 10 s revealed to be better, and the best results were obtained at a threshold of 75 HU. However, a matched-pairs analysis of patients matched for gender and age, examined with a standard delay, showed only a trend for a superior timing of the arterial phase with the use of bolus tracking. This might be due to the fact that triggering on the contrast enhancement of the abdominal aorta neglects differences of the mesenteric blood flow caused by weight or portal haemodynamics such as hypertension or truncal stenosis. The additional influence of age that was also shown by the significant decrease of percentual liver enhancement with age should

have been removed by the matched-pairs analysis. Furthermore, there are still individual changes in bolus characteristics caused by passage through the lungs and heart. These and other influences seem to have such a high physiological variability that even only 41 % of the examinations with an optimal trigger protocol show an optimal contrast enhancement in the arterial phase. Even a wider definition of optimal arterial enhancement is met by only 60 % of the patients.

These results stand in contrast to the results of Kopka et al., who found sufficient timing in 93 % of the patients examined with bolus tracking [9]. Their ROI was also placed into the descending aorta (but at the level of the heart), an 8-s delay after triggering was used and 120 ml contrast agent at a flow of 4 ml/s was injected. However, a different definition of an optimal arterial phase was used: the onset was defined as a splenic parenchymal enhancement of 10 HU, and the end was marked by any decrease of enhancement in the aorta or enhancement in the liver parenchyma of more than 20 HU. With our patients, there was only a moderate correlation between early contrast enhancement of the spleen and of the liver. Therefore, enhancement of the spleen was not used as a criterion of optimal contrast of the arterial phase, even if both liver and spleen have a similar perfusion rate of 1 ml g^{-1} min^{-1} [2, 9]. Since the maximum hepatic contrast enhancement is delivered by both arterial (25 %) and portal venous (75 %) blood flow, a hepatic enhancement of 20–30 % compared with the maximum reached in the portal venous phase can be considered as reflecting nearly exclusive arterial blood supply [5, 10]; thus, this hepatic enhancement was chosen as the criterion of an optimal arterial phase.

In order to solve the problems resulting from indirect triggering on the aorta, one might suggest direct triggering either on the hepatic artery or hepatic parenchyma. Yet, detection of the hepatic artery in the unenhanced examination is not always possible, and its position varies within the respiration cycle. For triggering on the parenchyma, on the other hand, a reliable detection of a very small density increase over baseline would be necessary, because the mean enhancement of the liver in the arterial phase is 13 HU, and after triggering at least 5 s are needed to initiate scanning; therefore, placement of the ROI into the abdominal aorta seems to be more robust at present. Furthermore, even patients with an optimal average early hepatic enhancement between 20 and 30 % show significant differences for the different analysed regions. Enhancement of the cranial and middle section of the right liver lobe is significantly lower than the left liver lobe and the caudal section of the right liver lobe. This is not only caused by the craniocaudal scan direction but also by the arterial liver perfusion. As the arterial phase is much shorter than the portal venous phase, faster scanning of the whole liver would be necessary. These technical problems, the need for a shorter scan delay after triggering as well as for a faster scanning, hopefully can be solved with the new multislice CT scanners.

Limitations of this study

A potential bias of our study is the retrospective analysis of the control group examined with a standard delay. This was accepted in order to establish a larger study group consisting of patients matched for gender and age. No differentiation for height, weight, cardiac or liver diseases was made, because, firstly, the large study population was expected to equalize the number of patients with different characteristics within both study groups, and, secondly, it was our intention to evaluate bolus tracking in a routine clinical setting in a non-selected patient population. Further potential criticism is that a fixed contrast-injection protocol of 120 ml contrast material and a flow of 3 ml/s was used as is usual with our department. However, using this injection rate for the assessment of the arterial phase is in concordance to literature [20] and is also used for dynamic CT of hepatocellular carcinoma [21]. We also used a fixed delay of 60 s for the initiation of scanning for the portal venous phase after triggering. Although this delay (the MTT of 15 s has to be added) is comparable to the optimal time delays described in the literature [18, 22, 23], it may be possible that the portal venous phase did not always meet the maximum contrast enhancement of the liver.

Conclusion

There are significant differences in the success of automatic bolus tracking with the use of different thresholds and delays after trigger. However, there is only a trend for a superior timing with the use of bolus tracking compared with the use of a standard delay. Therefore, optimal imaging of the arterial phase cannot be achieved in each patient by triggering on the abdominal aorta using the protocols that were presented in this study probably due to individual differences in the arterial blood supply of the liver.

References

1. Baron LR (1994) Understanding and optimizing use of contrast material for CT of the liver. Am J Roentgenol 163: 323–331
2. Lutz J, Henrich H, Bauereisen E (1975) Oxygen supply and uptake in the liver and the intestine. Pflugers Arch 360: 7–15
3. Glazer GM, Aisen AM, Francis IR, Gross BM, Gyves JW, Ensminger WD (1986) Evaluation of focal hepatic masses: a comparative study of MRI and CT. Gastrointest Radiol 11: 263–268
4. Mitchell DG (1997) Contrast enhancement for the abdomen and pelvis. Eur Radiol 7(Suppl 5):238–242
5. Silverman PM, Brown B, Wray H, Fox SH, Cooper C, Roberts S, Zeman RK (1995) Optimal contrast enhancement of the liver using helical (spiral) CT: value of SmartPrep. Am J Roentgenol 164: 1169–1171
6. Kopka L, Funke M, Fischer U, Vosshenrich R, Oestmann JW, Grabbe E (1995) Parenchymal liver enhancement with bolus-triggered helical CT: preliminary clinical results. Radiology 195: 282–284
7. Silverman PM, Roberts SC, Ducic I, Tefft MC, Olson MC, Cooper C, Zeman RK (1996) Assessment of a technology that permits individualized scan delays on helical hepatic CT: a technique to improve efficiency in use of contrast material. Am J Roentgenol 167: 79–84
8. Silverman PM, Roberts S, Tefft MC, Brown B, Fox SH, Cooper C, Zeman RK (1995) Helical CT of the liver: clinical application of an automated computer technique, SmartPrep, for obtaining images with optimal contrast enhancement. Am J Roentgenol 165: 73–78
9. Kopka L, Rodenwaldt J, Fischer U, Mueller DW, Oestmann JW, Grabbe E (1996) Dual-phase helical CT of the liver: effects of bolus tracking and different volumes of contrast material. Radiology 201: 321–326
10. Frederick MG, McElaney BL, Singer A, Park KS, Paulson EK, McGee SG, Nelson RC (1996) Timing of parenchymal enhancement on dual-phase dynamic helical CT of the liver. How long does the hepatic arterial phase predominate? Am J Roentgenol 166: 1305–1310
11. Yamashita Y, Mitsuzaki K, Yi T, Ogata I, Nishiharu T, Urata J, Takahashi M (1996) Small hepatocellular carcinoma in patients with chronic liver damage: prospective comparison of detection with dynamic MR imaging and helical CT of the whole liver. Radiology 200: 79–84
12. Mitsuzaki K, Yamashita Y, Ogata I, Nishiharu T, Urata J, Takahashi M (1996) Multiple-phase helical CT of the liver for detecting small hepatomas in patients with liver cirrhosis: contrast-injection protocol and optimal timing. Am J Roentgenol 167: 753–757
13. Birnbaum BA, Jacobs JE, Yin D (1995) Hepatic enhancement during helical CT: a comparison of moderate rate uniphasic and biphasic contrast injection protocols. Am J Roentgenol 165: 853–858
14. Small WC, Nelson RC, Bernardino ME, Brummer LT (1994) Contrast-enhanced spiral CT of the liver: effect of different amounts and injection rates of contrast material on early contrast enhancement. Am J Roentgenol 163: 87–92
15. Hollett MD, Jeffrey RB Jr, Nino-Murcia M, Jorgensen MJ, Harris DP (1995) Dual-phase helical CT of the liver: value of arterial phase scans in the detection of small (≤1.5 cm) malignant hepatic neoplasms. Am J Roentgenol 164: 879–884
16. Van Hoe L, Marchal G, Baert AL, Gryspeerdt S, Mertens L (1995) Determination of scan delay time in spiral CT-angiography: utility of a test bolus injection. J Comput Assist Tomogr 19: 216–220
17. Rubin GD, Alfrey EJ, Dake MD, Semba CP, Sommer FG, Kuo PC, Dafoe DC, Waskerwitz JA, Bloch DA, Jeffrey RB (1995) Assessment of living renal donors with spiral CT. Radiology 195: 457–462
18. Dinkel HP, Fieger M, Knupffer J, Moll R, Schindler G (1998) Optimizing liver contrast in helical liver CT: value of a real-time bolus-triggering technique. Eur Radiol 8: 1608–1612
19. Paulson EK, Fisher AJ, DeLong DM, Parker DD, Nelson RC (1998) Helical liver CT with computer-assisted bolus-tracking technology: Is it possible to predict which patients will not achieve a threshold of enhancement? Radiology 209: 787–792
20. Shimizu T, Misaki T, Yamamoto K, Sueyoshi K, Narabayashi I (2000) Helical CT of the liver with computer-assisted bolus-tracking technology: scan delay of arterial phase scanning and effect of flow rates. J Comput Assist Tomogr 24: 219–223
21. Pacella CM, Bizzarri G, Anelli V, Valle D, Fabbrini R, Bianchini A, Fenderico P, Rossi Z (1998) Evaluation of the vascular pattern of hepatocellular carcinoma with dynamic computed tomography and its use in identifying optimal temporal windows for helical computed tomography. Eur Radiol 8: 30–35
22. Silverman PM, O'Malley J, Tefft MC, Cooper C, Zeman RK (1995) Conspicuity of hepatic metastases on helical CT: effect of different time delays between contrast administration and scanning. Am J Roentgenol 164: 619–623
23. Silverman PM, Cooper C, Trock B, Garra BS, Davros WJ, Zeman RK (1995) The optimal temporal window for CT of the liver using a time–density analysis: implications for helical (spiral) CT. J Comput Assist Tomogr 19: 73–79