Pharmacokinetic Compartment Modeling 을 이용한 나선식 CT 에서의 간암-간 대조 곡선의 Simulation

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Simulation of lesion-to-liver contrast difference curves in Dynamic Hepatic CT with Pharmacokinetic Compartment Modeling

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ABSTRACT

Contrast-enhanced CT has an important role in the assessment of liver lesions. However, the optimal protocol to get most effective result is not clear. The main principle for deciding injection protocol is to optimize lesion detectability by rapid scanning when lesion-to-liver contrast is maximum. For this purpose, we developed a physiological model of contrast medium enhancement based on the compartment modeling and pharmacokinetics. Blood supply to liver was modeled in two paths. This dual supply character distinguishes the CT enhancement of liver from that of the other organs. The first path is by hepatic artery and the second is by portal vein. It is assumed that only hepatic artery can supply blood to hepatocellular carcinoma (HCC) compartment. It is known that this causes the difference of contrast enhancement between normal liver tissue and hepatic tumor. By solving differential equations for each compartment simultaneously using computer program Matlab, CT contrast-enhancement curves were simulated. Simulated enhancement curves for aortic, hepatic, portal vein, and HCC compartments were compared with mean enhancement curves from 24 patients exposed to the same protocols as simulation. These enhancement curves were in a good agreement. Furthermore, we simulated lesion-to-liver curves for various injection protocols, and analyzed the effects. These may help to optimize the scanning protocols for good diagnosis.

I. INTRODUCTION

Many abdominal CT applications necessitate intravenous administration of contrast medium to enhance lesion conspicuity. However, the optimal technique for injection is not clear. we should find the protocol not only to maximize contrast difference between normal and abnormal tissue resulting from a nonequal distribution of contrast media but also to elongate the time period during which the lesion detection is clear. Contrast media enhanced tumor identification can be performed either according to the vascularization of the lesion, or by using the permeability of the endothelium and the accessible extravascular space [1]. Because of the extracellular distribution of contrast media, rapid extravasation occurs and compounds leave the vascular compartment within seconds after injection and equilibrate in the total extracellular space [1]. The separate characterization of intravascular space and tissue parenchyma is possible only to a very limited extent because of the rapid extravasation process. In case the tumor is hypervascular, the chance to detect the lesion become high if imaging is performed during vascular phase. On the other hand, diffusion of contrast material into the extravascular space is a slower process in hypovascular metastases than in normal hepatic parenchyma [2]. That is, metastatic liver nodules of colorectal carcinoma are usually hypodense on contrast CT images so that maximum detectability may be attained at the peak enhancement of the liver [3]. To investigate the effect of injection parameters of contrast medium on enhancement at computed tomography, we developed a pharmacokinetic model and simulated the resulted contrast enhancement.

II. Materials and Methods

Intravenously administrated contrast medium (through an antecubital vein) is mixed in the right side of the heart and distributed through the vascular compartment and it is diffused rapidly to the extracellular compartment. Because CT contrast medium does not penetrate cells in general, the intracellular part of liver remains essentially free of contrast medium. Therefore we can neglect the intracellular compartment in the model. Contrast medium is eliminated by urine at a constant rate [5]. The average blood volume for a typical adult was set to 5L (3L of plasma and 2L of red blood cells) and the average cardiac output to be 6.5L/min. The governing equation for this blood vessel compartment can be derived from mass conservation of contrast material, that is

$$V\frac{dC}{dt} = \sum q_{in} \cdot C_{in} - \sum q_{out} \cdot C \quad , \quad (1)$$

where C is the concentration of the contrast material of the compartment and C_{in} is that of the former compartment. In the model of organs, we must add one additional compartment representing the extracellular space of the organ to the capillary vessel compartment. In the capillary vessel compartments, contrast materials are exchanged by two mechanisms. One is by volumetric blood flow like equation (1), and the other is by diffusion through capillary membranes that permits the exchange of materials among the capillary and extracellular space. Therefore the governing equation for the capillary compartment is,

$$V\frac{dC}{dt} = \sum q_{in} \cdot C_{in} - \sum q_{out} \cdot C - p \cdot s \cdot (C - C_{ec}), (2)$$

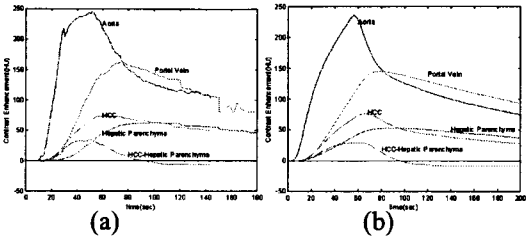
where C_{ec} is the concentration of extracellular compartment, p is permiability of vessel membrane, and s is diffusion surface area. By solving differential equations for each compartment simultaneously, we can get the contrast medium concentration in each compartment. We referred the result of Bae[5] for the relationship between CT enhancement and concentration. For simplicity, only the compartments having direct relations with the blood supply to liver is designated. Blood is supplied to liver by two paths. This dual supply character distinguishes the CT enhancement of liver from that of the other organs. The first path is by hepatic artery and the second is by portal vein. In case hepatic lesion exists, it is regarded as independent compartment characterized by its vascularity and volume. It is assumed that only hepatic artery can supply blood to this compartment. It is known that this causes the difference of contrast enhancement between normal liver tissue and hepatic tumor.

Simulations were performed for the physiological parameters of typical adults. These parameters can be varied, if we know the total blood volume and cardiac output for the indivisual patient. According to the sex, weight (w in pounds), and height (h in inches) of given patient, the blood volume is calculated by $33.164 \times h^{0.725} \times w^{0.425} - 1{,}229$ for a man, and by $33.164 \times h^{0.725} \times w^{0.425} - 1{,}954$ for a woman. The equation for cardiac output is $36.36 \times h^{0.725} \times w^{0.425}$ both for a woman and a man [4].

III. Results

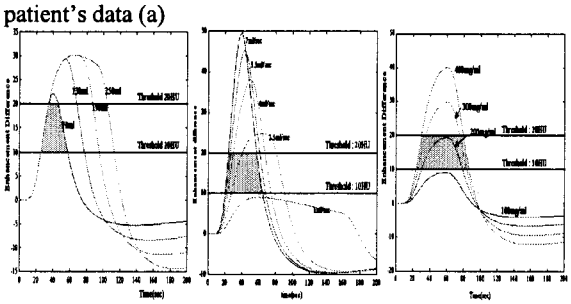
Contrast medium concentration as a function of time was obtained by solving all the governing equations simultaneously. Figure 1 shows a simulated example for contrast medium concentration in aorta and liver parenchyma after injection of 150ml of contrast medium with the concentration of 300mg/ml. The injection rate was set to 3ml/sec. individual enhancement curves were obtained for 24 patients (21 men and 3 women aged 35-75 years) who allowed the same anatomic level to be scanned throughout the examination and then averaged at each time point over all 24 patients. We obtained mean attenuation values for the tumor, hepatic parenchyma, aorta, and portal vein. And then, the attenuation difference between the tumor and hepatic parenchyma was plotted to find the region of best conspicuity. The simulated enhancement curves generated from the model were in a good agreement with the mean enhancement curves observed in patients [fig 1 (a), (b)]. The simulated and empiric enhancements have maximum values respectively 235.3 HU, and 244.1 HU in aorta, and 76.2HU, 74.8 HU in HCC. The mean difference in maximum enhancement was 4.7% for the aortic curve and 9.7% for the hepatic curve.

We simulated HCC-to-Liver contrast curve in various injection protocols and figure 2 shows how conspicuity varies according to changed protocol.



(a) (b)

[Figure 1] Comparison of simulation curves(b) with patient's data (a)



[Figure 2] HCC-to-Liver contrast curve in various injection protocols. left: injection volume change, center: injection rate change, right: concentration change

IV. Conclusion

The delivery of contrast material to the liver after peripheral intravenous injection is influenced by numerous factors. We developed a physiological model of contrast medium enhancement containing HCC compartment. Blood supply to liver was modeled in two paths. The first path is by hepatic artery and the second is by portal vein. It is assumed that only hepatic artery can supply blood to hepatocellular carcinoma (HCC) compartment. To test the utility of this model, we compared simulation results with clinical data obtained from 24 patients at the same condition. And then analyzed the effects of various injection protocols on hepatic lesion detectability. These may help to optimize the scanning protocols for good diagnosis.

V. References

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