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# Does apparent diffusion coefficient predict the degree of liver regeneration of donor and recipient after living donor liver transplantation?

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ABSTRACT

*Objective:* To elucidate the relationship between the ADCs of the liver graft and the remnant liver and the degree of liver regeneration in LDLT.
*Materials and methods:* 15 recipients and 15 corresponding donors underwent magnetic resonance imaging and computed tomography 1–2 weeks after living donor liver transplantation (LDLT). For diffusion-weighted imaging (DWI), a single-shot echo-planar sequence with b-factors of 0, 500, and 1000 s/mm$^2$ was scanned. ADCs of the liver parenchyma were calculated at b factors of 0 and 500 and 1000 (ADC 0–500–1000) or 0 and 500 (ADC 0–500) or 500 and 1000 (ADC 500–1000). The liver volume ratio at LDLT, the mean ADCs and the regeneration rate were compared between the graft and the remnant liver using paired-t tests.
*Results:* The mean liver volume ratio of the recipients (41.3 ± 9.8%) tended to be smaller than that of the donors (51.8 ± 13.8%). The mean ADC 0–500 of the remnant liver (1.72 ± 0.33) was significantly higher than that of the graft (1.43 ± 0.32). The regeneration rate of the graft (2.07 ± 0.41) was significantly higher than that of the remnant liver (1.53 ± 0.49).
*Conclusion:* ADC 0–500 can describe differences in blood perfusion between liver grafts and the remnant liver according to the degree of liver regeneration.



## 1. Introduction

Chronic liver disease is a major public health problem worldwide, and its chronic damage leads to cirrhosis and liver failure [1]. Living donor liver transplantation (LDLT) is the standard therapy for decompensated liver cirrhosis. Many factors that can be used to evaluate the postoperative course of an LDLT recipient have been reported [2], and one of them is regeneration of the liver graft (recipient liver) or the remnant liver (donor liver). In general, the degree of liver regeneration can be estimated using computed tomography (CT) volumetry [3]. In contrast to CT, magnetic resonance (MR) imaging, in addition to being a non-invasive modality that shows biological morphology, also gives us functional information. Of many MR sequences, the signal intensity (SI) of diffusion-weighted imaging (DWI) and the apparent diffusion coefficient (ADC) have been reported to be associated with cellular density as well as intra- or extracellular edema and viscosity [4]. We therefore hypothesized that the ADCs of the liver graft and the remnant liver might reflect the degree of regeneration.

The purpose of this study was to elucidate the relationship between the ADCs of the liver graft and the remnant liver and the degree of liver regeneration in LDLT.

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## 2. Materials and methods

### 2.1. Study population

Institutional review board approval was obtained (blind), and the requirements for informed consent were waived for this retrospective study. From January 2011 to December 2012, 76 recipients underwent LDLT at our institution. The following criteria were used for inclusion in this study: (a) Both recipients and donors underwent MRI and CT at 1–2 weeks after LDLT; (b) MRI was scanned using 1.5T MRI scanner. 52 cases were excluded because they did not undergo MRI. 9 cases were excluded because recipients or donors underwent MRI examination using 3T MRI scanner. Finally, 15 recipients and 15 corresponding donors were enrolled in our study. The donors were 6 men and 9 women (age range, 26–59 years; mean age, 40 years). The recipients were 6 men and 9 women (age range, 23–64 years; mean age, 52 years). Their Child-Pugh grades were grade B in two and grade C in 13 recipients. Left and right lobes were transplanted in 7 and 8 recipients, respectively. In our institute splenectomy is basically performed in LDLT recipient and was performed for 14 recipients in this study. The remaining one recipient, who was 27-year-old man with a history of kasai procedure for biliary atresia at infant, did not undergo splenectomy. There was no remarkable event during or after any LDLT.

### 2.2. MR imaging

After LDLT each patient underwent a gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced MR examination using a whole-body 1.5T scanner (Intera Achieva Nova Dual; Philips Medical Systems, Best, The Netherlands) equipped with a four-element sensitivity encoding (SENSE) body coil. Imaging included axial fat-suppressed T2-weighted fast spin-echo, axial dual-echo T1-weighted fast field-echo, axial DWI, and axial three-dimensional T1 high-resolution isotropic volume excitation (3D THRIVE) which was scanned before and 20 min after a single intravenous injection of 0.1 mL/kg (total amount: 4.3–8.4 mL) of Primovist (Bayer Schering Pharma, Osaka, Japan). All sequences covered the whole liver.

The imaging parameters of the axial DWI were as follows: respiratory trigger, single-shot echo-planar imaging, repetition time (TR)/echo time (TE) = 1542 ms/71 ms, 128 × 73 matrix, 36 × 30.4 cm field of view (FOV), 7-mm section thickness, 1-mm intersection gap, 0.7 half scan factor, one signal average, spectral presaturation inversion recovery, SENSE factor = 2, b-factors of 0, 500, and 1000 s/mm$^2$, diffusion gradients applied in three axes, 25 sections acquired and 1.54 min acquisition time.

ADC maps were automatically generated on the operating console using images scanned with b-factors of 0, 500, and 1000 s/mm$^2$. The imaging parameters of 3D THRIVE were as follows: TR/TE/flip angle = 3 ms/1 ms/20°, matrix 224 × 116, FOV 36 cm, rectangular field of view (RFOV) 75%, SENSE factor 1.3, slice thickness 4 mm (2 mm with interpolation), centric k-space ordering, spectral presaturation inversion recovery, acquired 80 sections, scan time 18 s, and breath-holding.

### 2.3. CT imaging

Donors underwent a CT examination for the preoperative volumetry examination using a 64 multi detector-row (MD) CT scanner (Aquilion 64, Toshiba Medical, Tokyo). The scanning was performed before and after the administration of 1.62 mL/kg (total amount: 70–125 mL) of iodinated contrast medium (Iopamiron 370; Bayer Schering Pharma). The contrast was administered intravenously for 20 s. Contrast-enhanced images were obtained during the early arterial phase (real prep), the arterial phase (15 s after the first phase), the portal venous phase (70 s after the initiation of the injection), and the delayed phase (90 s after the injection initiation). The imaging acquisition parameters were as follows: voltage, 120 kV; electric current, automatic; collimation, 0.5 mm; image reconstruction thickness, 1 mm (early arterial phase and portal venous phase) or 2 mm (non-contrast phase, arterial phase, and delayed phase); and helical pitch, 53.

After LDLT recipients and donors underwent CT examination within 2 days before or after the MR examination using a 64-MDCT scanner (Aquilion 64, Toshiba Medical, Tokyo). The scanning was performed before and after the administration of 100 mL of iodinated contrast medium (Iopamiron 370; Bayer Schering Pharma, Osaka, Japan, or Omnipaque 350; Daiichi-Sankyo, Tokyo). The contrast was intravenously administered at a rate of 3 mL/s. Contrast-enhanced images were obtained during the arterial phase (43 s after the initiation of the injection), the portal venous phase (70 s after the injection initiation), and the delayed phase (240 s after the initiation of the injection). The imaging acquisition parameters were: voltage, 120 kV; electric current, automatic; collimation, 0.5 mm; image reconstruction thickness, 5 mm; and helical pitch, 53.

### 2.4. Imaging analysis

In a consensus fashion, two radiologists (A.N. and K.M.) measured the ADCs of the liver graft and the remnant liver by placing a region of interest (ROI) on the ADC map. They placed as large an ROI as possible while avoiding artifacts and blood vessels. For the left lobe graft or remnant liver, they placed the ROI at the inferior portion of the medial segment to avoid artifacts due to cardiac motion. We defined the ADC obtained in this manner as ADC 0–500–1000.

The SI of each liver parenchyma was also measured on DWI images with b-factors of 0, 500 and 1000 s/mm$^2$. The same-sized ROI was placed at the same location on the ADC map and three types of DWI images. ADCs were also calculated using the two b-factors of 0 and 500 s/mm$^2$ or 500 and 1000 s/mm$^2$. We defined them as ADC 0–500 and ADC 500–1000, respectively.

The liver volume ratio of each recipient and donor was calculated using following formulas: the actual graft volume/standard liver volume (SLV) × 100(%) for the recipient, and the remnant liver volume/preoperative CT liver volume × 100(%) for the donor. The SLV was calculated using the following formula: SLV = 706.2 × body surface area +2.4 [5].

The postoperative MR liver volume was calculated from axial 3D THRIVE images after Gd-EOB-DTPA-enhancement using a workstation (Volume analyzer SYNAPSE VINCENT, Fuji Film Medical, Tokyo). The regeneration rate of the liver was calculated using the following formula: postoperative MR liver volume/the graft liver volume at LDLT for recipient and postoperative MR liver volume/the remnant liver volume at LDLT for donor. Preoperatively, the remnant liver volume was also estimated on donor CT according to scheduled operative methods, using the same workstation. For the liver graft volume, the actual values measured during LDLT were used.

### 2.5. Statistical analysis

The liver volume ratio of the recipients was compared with that of the donors. The mean ADCs and regeneration rate were compared between the liver graft and the remnant liver and also between left lobe and right lobes for the liver grafts and the remnant livers. A paired-t test was used for these statistical analyses. The correlations between the three types of ADC and the regeneration rate of the left lobe or the right lobe were evaluated by respective regression analyses. A p-value < 0.05 was considered significant.