Article focus
We hypothesized that Indocyanine green (ICG) fluorescence angiography can be used to evaluate the blood flow of the rotator cuff tendon.

By comparison with normal rotator cuffs, we hypothesized that the blood flow of torn rotator cuffs is decreased, while that of rotator cuff in patients with adhesive capsulitis is increased.

Key messages
ICG fluorescence angiography allowed for evaluation of real-time blood flow of the rotator cuff in arthroscopic surgery.

The adhesive capsulitis group showed significantly earlier enhancement than the normal rotator cuff group and rotator cuff tear group. In addition, the adhesive capsulitis group had a significantly smaller hypovascular area ratio.
hypoventricular area ratio than the normal rotator cuff group and rotator cuff tear group.

- There were no significant differences in the time to enhancement and hypoventricular area ratio between the normal rotator cuff group and rotator cuff tear group.

**Strengths and limitations**

- This is the first study to evaluate the *in vivo* real-time blood flow of the rotator cuff tendon using ICG fluorescence angiography from the articular side.
- The number of patients in each group was small, and there was a predominance of men in this study.
- Patient age in the normal rotator cuff group was not consistent with that in the other groups.
- We did not observe blood flow of the rotator cuff tendon from the bursal side.

**Introduction**

Blood flow abnormalities are among the most crucial factors in degenerative rotator cuff tears and adhesive capsulitis. In patients with degenerative rotator cuff tears, vascular insufficiency of the supraspinatus tendon has been proposed as one cause of the tear.\(^1\)\(^4\) Blood flow has also been considered as an essential factor for healing of the rotator cuff tendon.\(^5\) In patients with adhesive capsulitis, increased blood flow in both the rotator interval and axillary pouch has been reported based on dynamic MRI. An association between increased blood flow and pain has also been recognized as a process that occurs during exercise.\(^6\) In addition, embolization of increased blood vessels in the rotator interval can reportedly relieve pain and restore shoulder function.\(^7\) Thus, information about blood flow is important in order to understand the pathophysiology of shoulder diseases and to identify treatment strategies.

Doppler ultrasound and laser Doppler flowmetry (LDF) have been attempted as blood flow assessment techniques in clinical practice. Although various studies have utilized LDF and Doppler ultrasound, such techniques require another probe in addition to the scope and may not be easily applied in routine surgery.\(^8\)\(^-\)^\(^11\)

Indocyanine green (ICG) fluorescence angiography is an emerging technique that can provide detailed anatomical information during surgery. It has been used for visual evaluation of intraoperative blood flow in various surgical fields, such as cardiac surgery and transplant surgery.\(^12\)\(^,\)^\(^13\) In the orthopaedic field, Kim et al\(^14\) reported differences in perfusion of the rabbit’s rotator cuff tendon between parallel-type transosseous repair and suture-bridge configuration repair in the early phase using ICG fluorescence angiography. However, whether ICG fluorescence angiography can be used to evaluate the blood flow of the rotator cuff tendon in the clinical setting remains unknown. A new optical system that can be integrated into a surgical microscope or endoscope was recently developed, and ICG fluorescence angiography has been applied to the fields of neurosurgery and laparoscopic surgery.\(^12\)\(^,\)^\(^15\) To our knowledge, no clinical studies based on arthroscopic ICG fluorescence angiography have been published.

We hypothesized that ICG fluorescence angiography can be used to evaluate the blood flow of the rotator cuff tendon in arthroscopic surgery. In addition, by comparing with normal rotator cuffs, we hypothesize that the blood flow of torn rotator cuffs is decreased, while that of rotator cuffs in patients with adhesive capsulitis is increased. The first purpose of this study was to clarify whether the blood flow of the rotator cuff can be visually recognized by ICG fluorescence angiography. The second purpose was to evaluate differences in blood flow among patients with rotator cuff tears, normal rotator cuffs, and adhesive capsulitis using ICG fluorescence angiography.

**Materials and Methods**

**Patients.** This prospective study was approved by our institutional review board, and informed consent was obtained from all participating patients. For patients aged less than 20 years, informed consent was obtained from both the patients and their parents.

The following patients were included in the study: those undergoing arthroscopy for a rotator cuff tear; those with a normal rotator cuff but undergoing arthroscopy for a condition unrelated to rotator cuff disease, such as instability or labral tears; and those undergoing arthroscopy for adhesive capsulitis. The following patients were excluded from the study: those who were younger than 15 years; had undergone shoulder surgery; had received intra-articular steroid injections; had comorbidities that may affect microvascular blood flow (e.g., diabetes, cardiovascular disease, local infection, osteoarthritis or fractures); or had large/massive rotator cuff tears. A large-to-massive tear was defined by an anteroposterior or mediolateral diameter of >3 cm on preoperative MRI using the classification established by DeOrio and Cofield.\(^16\) Patients were diagnosed by an experienced senior shoulder surgeon (TI) based on the history of their present illness, physical examination findings, and image findings (plain radiograph and MRI). Patients with a normal rotator cuff or adhesive capsulitis were confirmed to have no rotator cuff tear by preoperative MRI and at the time of surgery.

The indications for operative treatment of rotator cuff tears or adhesive capsulitis were shoulder pain and failure of conservative treatment. The indications for operative treatment of instability or labral tears were a feeling of functional impairment during activities of daily living and sports participation. All patients had been experiencing symptoms for a minimum of three months and had
previously undergone a course of conservative management that included medication and physical therapy.

From October 2016 to December 2017, a total of 42 consecutive patients (33 male, nine female) undergoing arthroscopy for a rotator cuff tear, a condition unrelated to rotator cuff disease such as instability and labral tear, and patients undergoing arthroscopy for adhesive capsulitis were enrolled. Large/massive rotator cuff tears were excluded because the long head of the biceps brachii (LHB) was damaged or the observable area was small due to retraction of the cuff stump (16 patients). The remaining 26 patients (23 male, three female) were included in this study. The participants were categorized into three groups based on their diagnoses: the rotator cuff tear group (ten patients); normal rotator cuff group (eight patients); and adhesive capsulitis group (eight patients).

**ICG fluorescence angiography.** ICG fluorescence angiography was performed using a near-infrared endoscope system (D-Light P System; Karl Storz SE & Co. KG, Tuttingen, Germany). This device is a special camera system that can perform ICG fluorescence angiography and is usually used for laparoscopic surgery. ICG (Diagnostics; Daiichi-Sankyo Pharmaceutical, Tokyo, Japan) was intravenously injected at 0.2 mg/kg body weight and became instantly bound to globulins in the plasma. It is not metabolized in the body; it is excreted unchanged exclusively by the liver and has a plasma half-life of three to four minutes. ICG becomes fluorescent once excited by near-infrared light at wavelengths of about 820 nm; the absorption peak is around 807 nm, and the emission peak is around 822 nm. ICG fluorescence angiography can provide differentiation of vital anatomic structures from a few millimetres to more than 1 cm.

**Measurement area.** We observed the anterolateral region of the rotator cuff tendon. The LHB was used as an anatomical landmark to determine the constant measurement area. In the anteroposterior direction, the measurement area was determined from the anterior point of the rotator cuff tendon to 1 cm away posteriorly, near the LHB. The scope was set to the position at which observation could be performed from the anterior point of the rotator cuff tendon to 1 cm away posteriorly. In the normal rotator cuff group and adhesive capsulitis group, the measurement area of the rotator cuff tendon ranged from the bone attachment portion to the observable proximal area close to the LHB. In the rotator cuff tear group, the measurement area of the rotator cuff tendon ranged from the edge of the tear to the observable proximal area close to the LHB.

**Equipment.** A laparoscopic procedure (SPIES system, Karl Storz SE & Co.) was used in all cases. The imaging was provided by a high-end full high-definition camera system (IMAGE 1 SPIES) connected to a laparoscope with 0° field of direction, diameter of 5.8 mm, and length of 19 cm. A xenon light source (D-Light P SCB; Karl Storz SE & Co.) that provided both visible and near-infrared excitation light was used. Switching from standard light to near-infrared light was controlled by the surgeon using a foot switch. Visualization in both standard and near-infrared light was improved by a system for professional image enhancement (IMAGE 1 SPIES System), offering adjustable visualization modalities that could be selected according to the surgeon’s preferences. All operations were performed by one senior orthopaedic surgeon (TI) in our institution. The patients underwent general anaesthesia and were placed in the beach-chair position, and an interscalene nerve block was administered under ultrasonic echo guidance. The mean arterial pressure was maintained at 80 mmHg to 100 mmHg throughout the operation to maintain stable blood flow of the soft tissue. An irrigation pump was used throughout the procedure at 40 mmHg. The arm was positioned at 60° abduction, and a full arthroscopic assessment with a conventional arthroscope was performed through standard posterior portals. Next, an anterior portal infiltrated with lactated Ringer’s solution (Arthromatic; Baxter International Inc., Deerfield, Illinois) was created, and the arthroscope was switched to the near-infrared endoscope system. While the ICG was being injected by an anaesthetist, the surgeon switched from standard light to near-infrared light using a pedal. ICG fluorescence angiography was carried out, and the anterolateral region of the rotator cuff tendon was observed. The duration of time from switching to near-infrared light and the beginning of enhancement of the observed area was measured using video recordings. After injection of ICG, pictures were taken when the measurement area revealed enhancement. The video and image files of the ICG fluorescence angiography were stored on a computer hard drive and analyzed. The measurement area was calculated based on the distance in the anteroposterior direction of the rotator cuff tendon as a reference. The hypovascular area in the rotator cuff on the pictures during the maximum enhancement period was measured using ImageJ/Fiji 1.46 software (National Institutes of Health, Bethesda, Maryland), and the ratio of the hypovascular area to the total measurement area of the rotator cuff was calculated (Fig. 1). We defined this ratio as the hypovascular area ratio. We assessed the post-procedural adverse effects related to injection of ICG.

**Statistical analysis.** The measurements used to calculate the hypovascular area ratios were performed independently by two orthopaedic surgeons (ND and TI). The observers (ND and TI) were blinded to the patient information. The observers measured three times on different days, and the mean values were calculated. We calculated interclass correlation coefficients (ICCs) to measure interobserver agreement between the two surgeons and intraobserver reliability for one surgeon. Interobserver reproducibility for the hypovascular area ratios was also
evaluated by ICCs. All parameters were tested with normally distributed variables after initial assessment by Bartlett’s test. The differences in the mean age, measurement area, hypovascular area ratio, and enhancement time among the normal rotator cuff group, rotator cuff tear group, and adhesive capsulitis group were evaluated by one-way analysis of variance (ANOVA). The significance of the mean differences between the groups was evaluated by Tukey’s post-hoc test. Results are expressed as mean with 95% confidence interval (CI).

Results
Table I shows the demographics of the study population.

| Group                  | Male:Female | Mean age, yrs (range) |
|------------------------|-------------|-----------------------|
| RCT (n = 10)           | 9:1         | 58.5 (43 to 66)       |
| Normal (n = 8)         | 8:0         | 31.6 (19 to 65)       |
| Adhesive capsulitis (n = 8) | 6:2    | 55.4 (33 to 74)       |

RCT, rotator cuff tear

Anterolateral area of a rotator cuff tear observed at the time of indocyanine green (ICG) fluorescence angiography. a) The area surrounded by yellow lines is the area of the rotator cuff; this area was measured using ImageJ/Fiji 1.46 software. b) The area surrounded by yellow lines is the hypovascular area in the rotator cuff; this area was measured using ImageJ/Fiji 1.46 software. The ratio of the hypovascular area to the total area of the rotator cuff was calculated.

Discussion
This is the first study worldwide to examine the blood flow in the rotator cuff using ICG fluorescence angiography in vivo. We were able to evaluate differences in the blood flow in patients with various conditions, including rotator cuff tears, normal rotator cuffs, and adhesive capsulitis. Furthermore, this study is the first study to evaluate the blood flow of the rotator cuff from the articular side.

Evaluation of the cuff blood flow in vivo has been attempted in previous studies. LDF is the best-known method and allows for evaluation and quantification of blood flow in real time.9,10,19 However, the measurement is very sensitive to motion and contact pressure of the sensor tip applied by observers. Too much pressure may produce an ischaemic-like effect, while too little pressure may limit the depth of penetration of the laser, leading to a lack of signal output.19 Furthermore, to measure blood flow, it is necessary to bring the probe into close contact with the object, and only the immediate region can be evaluated. ICG does not require tissue contact, making it possible to observe a wider range than is possible with Doppler. In addition, the measurement involves only the
injection of ICG and observation; the observer’s skill itself seems to have only a small influence. In this study, the interobserver and intraobserver reliabilities had good agreement, since the evaluation is not a complicated measurement but simply a visual evaluation. This result is important because the operator will see and evaluate
during surgery. However, a dedicated scope system for ICG fluorescence angiography is required. If technological innovations continue to progress, we will be able to evaluate blood flow easily during surgery without switching the scope. Moreover, if we can check the blood flow of the cuff during surgery, we could clarify the difference in the cuff blood flow due to the suturing method and possibly be able to preserve the blood flow of the tendon at the time of surgery. In rotator cuff repair, re-tear occurs regardless of surgical method or suture method, and there are controversial issues on the factor of re-tear.20-22 If we can check the blood flow of the cuff during surgery, it would be useful for establishing an appropriate treatment for degenerative cuff tears. In addition, ICG fluorescence angiography can be applied to other operations such as surgical operations of other joints, tumours, debridement, and nonunion, but prospective studies and further development are needed to demonstrate the usefulness of ICG fluorescence angiography. Furthermore, ICG becomes fluorescent only where near-infrared light is applied. We can select which area we would like to observe, meaning no change to other areas. This is important as it means we can reduce the impact on assessing patient oxygenation. Although ICG fluorescence angiography involves a risk of allergy, we did not encounter patients with an allergy to ICG in this study.

A hypovascular area such as the critical zone was recognized near the bone insertion of the rotator cuff tendon in the normal rotator cuff group and rotator cuff tear group. Codman23 reported the presence of an ischaemic area (critical zone) proximal to the bone insertion of the supraspinatus tendon. The presence of a critical zone has been supported by several cadaver studies.24-26 Moseley and Goldie27 reported that the critical zone corresponded to the region of the anastomoses between the osseous and tendinous vessels. Our finding supports these previous anatomical studies.

The adhesive capsulitis group showed significant earlier enhancement and had a significantly smaller hypovascular area ratio than the normal rotator cuff group and rotator cuff tear group. Sasunoma et al6 reported that patients with adhesive capsulitis displayed increased clustering of blood flow and dispersion of contrast medium around the rotator interval and axillary pouch in the early phase compared with healthy volunteers using dynamic-enhanced MRI. They called this increased blood flow the “burning sign.” We directly observed the blood flow of the rotator cuff tendon from the articular side, and patients with adhesive capsulitis seemed to have increased blood flow in the supraspinatus tendon compared with patients with normal rotator cuffs and rotator cuff tears.

Patients in the normal rotator cuff group were younger than those in the rotator cuff tear group, but there was no significant difference in the hypovascular area ratio. Karthikeyan et al9 measured the microvascular blood flow in five different regions of the bursal side of the rotator cuff in four groups (normal rotator cuff, subacromial impingement, partial-thickness rotator cuff tear, and full-thickness rotator cuff tear) and found that the blood flow decreased in passing to the lateral part of the supraspinatus tendon in all groups. They demonstrated that the blood flow decreased in the lateral area of the rotator cuff tendon regardless of age. Our study also showed that a hypovascular area such as the critical zone is present in the rotator cuff from the articular side regardless of age. This might be related to the fact that the tendon adhesion rate after rotator cuff tear repair is not 100%. Bone marrow stimulation techniques have recently been reported to promote microvascularization of repair cuffs and to reduce the re-tear rate.28 This result may support the necessity of techniques in biologic augmentation on the footprint side.

There are several limitations in this study. First, the number of patients in each group was small, and there

| Group          | Mean hypovascular area ratio (95% CI) | Minimum | Maximum |
|----------------|--------------------------------------|---------|---------|
| RCT            | 0.3402 (0.2292 to 0.4512)            | 0.1836  | 0.6018  |
| Normal         | 0.3803 (0.2273 to 0.5333)            | 0.183   | 0.7053  |
| Adhesive capsulitis | 0.065 (0.019 to 0.1119)       | 0        | 0.179   |

| Group          | Mean enhancement time, seconds (95% CI) | Minimum | Maximum |
|----------------|----------------------------------------|---------|---------|
| RCT            | 65.0 (53.3 to 76.7)                    | 46.0    | 100.0   |
| Normal         | 66.5 (56.0 to 77.1)                    | 56.0    | 93.0    |
| Adhesive capsulitis | 27.6 (20.3 to 34.9)       | 18.0    | 45.0    |

CI, Confidence interval; RCT, rotator cuff tear
was a predominance of men in this study. A small number of measurements usually results in a low detection power. Although our number of measurements was small, the hypovascular area in the adhesive capsulitis group was significantly smaller than in the normal cuff and cuff tear groups. Second, the age of patients in the normal rotator cuff group was not consistent with that of patients in the other groups. Age should be matched in every group, and blood flow assessment should be done. However, in vivo studies have ethical considerations that introduce inevitable limitations. Patients were only invited to enroll if they required an arthroscopic operation for the treatment of their shoulder; they were not asked to participate for the purposes of the study alone. Among patients undergoing shoulder arthroscopic surgery, those with normal cuff tendons seem to have only instability or labral tears. Due to these unavoidable and ethical reasons, the normal rotator cuff group mainly comprised young patients undergoing stabilization or labral repair surgery. Third, we did not observe from the bursal side. Lohr and Uhthoff2 reported that the articular side of the rotator cuff is disadvantageous in terms of blood supply compared with the bursal side of the rotator cuff. If we had observed from the bursal side, there may have been differences in the enhanced area. However, this method is also applicable to the bursal side. Furthermore, it enables evaluation of blood flow of intra-articular lesions such as partial-thickness articular surface tears. Fourth, the field observation range was limited because we used a laparoscope with 0° field of direction. A 30° field of correction is often used in orthopaedic arthroscopy. Although there is a laparoscope with a 30° field of direction, the diameter is as large as 10 mm, increasing patient invasiveness. Therefore, we selected a laparoscope with a 0° field of direction and diameter of 5.8 mm that seemed to be less invasive. Fifth, several factors influenced the blood flow. In patients with instability or labral tears, blood flow may increase due to trauma. However, the operation was performed more than four months after the last dislocation. We think that this measurement could be done at a time when there is little or no influence by trauma. We used an irrigation pump to fill the glenohumeral joint during the operation. The pressure from the irrigation pump may have affected the blood flow measurement. However, the same irrigation pump pressure was applied to all patients. Additionally, all patients were under general anaesthesia with an interscalene nerve block administered under ultrasonic echo guidance. The blood vessels may have been dilated by the anaesthetic agent, increasing the blood flow. Furthermore, the blood flow may have changed depending on the body temperature and intraoperative position (beach-chair position or lateral decubitus position).

In conclusion, this is the first study to evaluate the in vivo real-time blood flow at the anterolateral area of the supraspinatus tendon using ICG fluorescence angiography from the articular side. The adhesive capsulitis group showed significantly earlier enhancement and had a significantly smaller hypovascular area ratio than did the normal rotator cuff group and rotator cuff tear group. The techniques of ICG fluorescence angiography are simple and easy to observe, observer reliability is high, and it has utility for evaluating blood flow during surgery.

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