

# Near-Infrared Fluorescence Imaging Can Help Identify the Contralateral Phrenic Nerve During Robotic Thymectomy

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**Purpose.** Unilateral robotic thymectomy is gaining popularity. Identifying the contralateral phrenic nerve is a key limitation to achieving maximal thymic tissue resection. We evaluated the feasibility and technique of fluorescence imaging on the daVinci-Si robot (Intuitive Surgical Inc, Sunnyvale, CA) to identify the contralateral pericardiophrenic neurovascular bundle (PNB).

**Description.** A unilateral right robotic thymectomy was performed in 10 patients. The thymus and its poles were mobilized. Indocyanine green was injected and fluoresced to identify the left PNB in four different viewing angles to assess the view that consistently positively identified the PNB.

**Evaluation.** No complications from indocyanine green or injuries to the phrenic nerve occurred. The contralateral PNB was visualized in 80% of patients from a left pleural view, infrequently from a mediastinal view, and never distal to the aortopulmonary window.

**Conclusions.** During right robotic thymectomy, fluorescence imaging facilitates identification of the contralateral phrenic nerve by fluorescing the pericardiophrenic vessels. It is best visualized from a left pleural view. This technology has the potential to maximize thymic tissue resection with a unilateral approach while reducing operative time and nerve injury.

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Minimally invasive thymectomy is gaining popularity and is an acceptable alternative to traditional transsternal and transcervical approaches for myasthenia gravis and small-sized thymomas [1, 2]. The goal of a minimally invasive thymectomy is to achieve a resection comparable to that of a transsternal thymectomy by removing the gland between both phrenic nerves and from the base of the diaphragm to the superior poles in the neck. Initially, unilateral video-assisted thoracoscopic surgical (VATS) approaches were attempted, but visualization of the contralateral phrenic nerve can be difficult. This led to the wider adoption of a bilateral VATS approach so that each phrenic nerve can be identified directly and all tissue removed with certainty [3].

Robotic-assisted thymectomy (RAT) is a promising new technique that has the potential to perform a complete thymectomy through a unilateral thoracic approach similar to a sternotomy or bilateral VATS [4]. Identification of the contralateral phrenic nerve may be easier with the improved visualization capabilities of the optical

system in the da Vinci robot (Intuitive Surgical Inc, Sunnyvale, CA) that uses 3-dimensional, high-definition vision and original magnification  $\times 10$ . Even with the robotic advantage, identification of the contralateral phrenic nerve can be challenging and time consuming. We evaluated the feasibility and technique of using indocyanine green (ICG) fluorescence imaging during RAT with the da Vinci Si robot to identify the contralateral phrenic nerve by visualizing the pericardiophrenic vasculature—the pericardiophrenic neurovascular bundle (PNB)—that runs parallel with the nerve.

## Technology

Near-infrared fluorescent imaging uses laser technology to activate an intravenously delivered agent, ICG, that when stimulated, can provide visualization of vascular structures. This technology was recently approved for use on the da Vinci Si HD Surgical System and has the potential ability to allow surgeons to view high-

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resolution near-infrared images of blood flow in macrovasculature and microvasculature as well as related tissue and organ perfusion in real-time during robotic surgical procedures.

ICG is a sterile, water soluble, tricarbo-cyanine dye with a peak spectral absorption at 800 to 810 nm in blood plasma or blood. After intravenous injection, ICG is rapidly and completely bound to large plasma proteins and thus remains intravascular, if vascular and capillary permeability are preserved, with a half-life of 2 to 5 minutes. It is exclusively metabolized by hepatic parenchymal cells and secreted entirely in bile. ICG is contraindicated in patients with a known iodide allergy, and its effects in pregnancy and on the fetus are unknown. Intraoperative ICG fluorescence imaging has been safely used for years and was initially found to be a simple and effective method to assess or identify vessels in a variety of surgical situations such as coronary artery graft patency [5], plastic [6] or transplant surgery [7]. The added cost of ICG is approximately \$80 based on the pharmacy purchase price.

### Technique

The institutional review board of Swedish Medical Center approved this study. Individual patient consent was waived.

#### Patients

This initial assessment of ICG fluorescence included 10 patients undergoing RAT for myasthenia gravis, with or without a thymoma, or thymoma alone.

#### Operative Technique

A right unilateral RAT was performed. Patients were positioned as previously described [2], with ports as follows: 12-mm camera in the fifth interspace in the anterior axillary line; robotic arm 1 (8.5 mm) in the fifth interspace in the midclavicular line, at least 10 cm away from the camera; and robotic arm 2 in the anterior axillary line at the fifth interspace just posterior to the edge of the pectoralis major

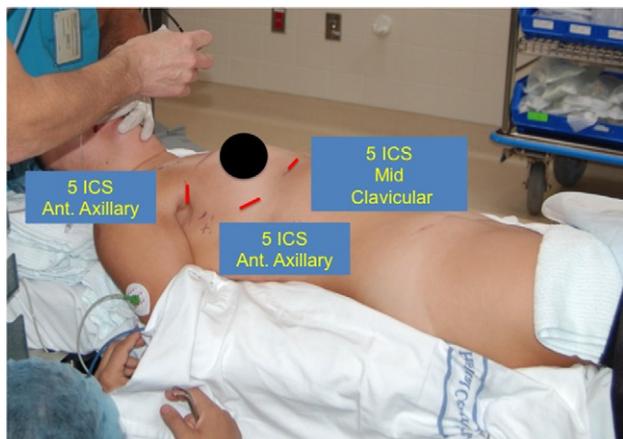


Fig 1. Patient positioning and port placement in the fifth intercostal space (5 ICS). (Ant. = anterior.)

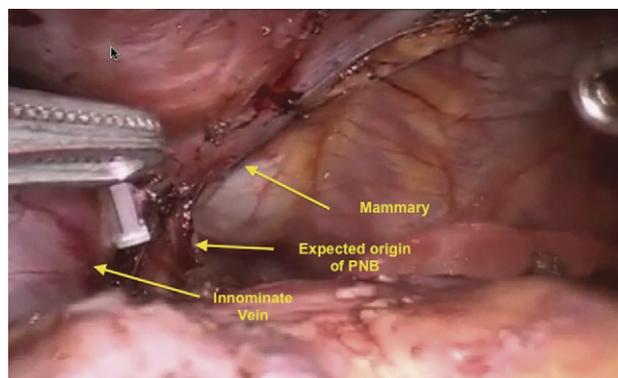


Fig 2. View of mammary-innominate vein complex. (PNB = pericardiophrenic neurovascular bundle.)

and guided by the internal view so that the trajectory line into the chest is inferior to the right internal mammary and vena caval junction (Fig 1).

Thymectomy was carried out in the following fashion. The mediastinal pleura was incised just anterior to the right phrenic nerve, continuing cephalad toward the mammary vein, then transitioning along the sternum and dividing the pleura along the mammary vessels. The areolar tissue against the sternum was bluntly dissected away until the left internal mammary vessels were visualized.

A 30-degree down scope was used to identify the confluence of the left mammary vessels and the innominate vein as a marker for the origin of the PNB (Fig 2). To identify the PNB, we used two different approaches:

In the first approach, the left pleura was left intact, and in succession, we dissected the right superior pole, and then the left superior pole was mobilized and the thymic vein(s) divided. Images were taken of the confluence of the mammary and innominate vessels to determine if we could identify the PNB (mediastinal view). The pleura was then opened widely to identify the PNB (Fig 3).

In the second approach, the pleura was opened widely as soon as the left mammary vessels were identified during the initial dissection. The right superior pole and then the left superior pole were mobilized in succession

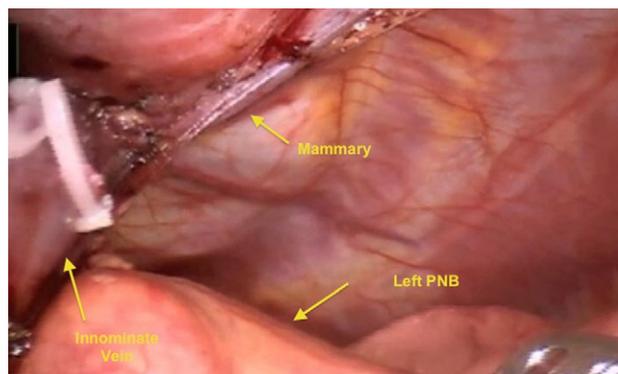


Fig 3. Pleural view of contralateral pericardiophrenic neurovascular bundle (PNB).

and the thymic vein(s) divided. Images were taken of the mediastinal and pleural views.

*Fluorescence Technique and Protocol*

To identify the PNB with fluorescence, we used a 6.25-mg bolus injection of ICG prepared with a sterile ICG solution into a peripheral venous catheter, immediately followed by a 10-mL bolus of normal saline. After changing the visual system to fluorescent mode, a fluorescence response in the mediastinal blood vessels and tissue was visible within 5 to 10 seconds after the injection. The fluorescent intensity reached its maximum approximately 1 minute after injection and then disappeared slowly. If repeated fluorescent images were required, they were taken with no less than 5 minutes between imaging sequences to allow much of the ICG to clear the area.

After ICG was injected, the resultant four views were recorded to identify the surrounding vessel complex and then the PNB from different viewing angles:

1. innominate vein–mammary vessels–pericardiophrenic vessel complex,
2. PNB from the mediastinal view,
3. PNB from the left pleural view, and
4. PNB distal to the aortopulmonary (AP) window.

After clear identification of the PNB, thymic mobilization and dissection were completed, and the thymus gland was removed in a retrieval bag through the enlarged camera port incision (3 to 5 cm). Extended removal, including the perithymic adipose tissue, was achieved through the unilateral thoracic access, and cervical access was not necessary in any case.

**Clinical Experience**

Near-infrared fluorescence imaging was used to evaluate 10 patients during RAT. Clinical characteristics, operative details, and outcomes are detailed in Table 1. The mean operative time was 191 minutes. No complications were observed from ICG, and no injuries occurred to the PNB, as determined by postoperative and follow-up chest roentgenograms.

Table 1. Study Population and Results

| Patient | Sex | Age (yrs) | Disease     | Size (cm) | BMI (kg/m <sup>2</sup> ) | Mammary Complex | View        |         |                     |
|---------|-----|-----------|-------------|-----------|--------------------------|-----------------|-------------|---------|---------------------|
|         |     |           |             |           |                          |                 | Mediastinal | Pleural | Distal to AP window |
| 1       | F   | 82        | Thymoma     | 5         | 21.6                     | N/A             | N/A         | +       | N/A                 |
| 2       | F   | 67        | Hyperplasia | ...       | 47.2                     | +               | —           | +       | —                   |
| 3       | M   | 31        | Thymolipoma | 3         | 30.1                     | +               | —           | —       | —                   |
| 4       | F   | 27        | MG          | ...       | 37.4                     | +               | —           | —       | —                   |
| 5       | F   | 52        | Thymoma     | 4         | 20.5                     | +               | —           | —       | —                   |
| 6       | M   | 20        | Hyperplasia | ...       | 34.2                     | +               | +           | —       | —                   |
| 7       | F   | 23        | MG          | ...       | 19.2                     | +               | —           | +       | —                   |
| 8       | M   | 33        | Hyperplasia | ...       | 34.1                     | +               | —           | +       | —                   |
| 9       | M   | 58        | Thymoma     | 10        | 26.7                     | +               | —           | +       | —                   |
| 10      | F   | 49        | Thymoma     | 9         | 23.6                     | +               | —           | +       | —                   |

“—” = not viewed; “+” = viewed.  
 AP = aortopulmonary window; BMI = body mass index; F = female; M = male; MG = myasthenia gravis; N/A = not applicable.

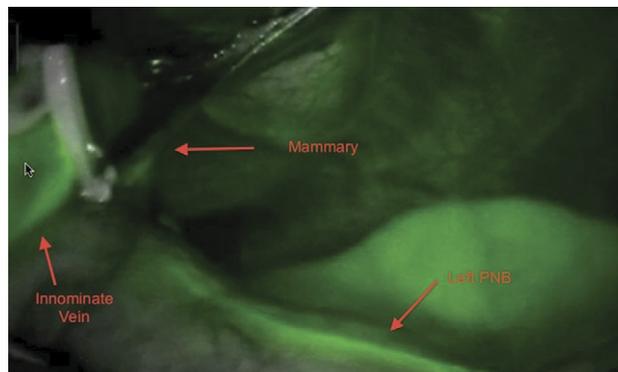


Fig 4. Pleural view of contralateral pericardiophrenic neurovascular bundle (PNB) under fluorescent imaging with indocyanine green.

In patient 1, we validated as proof-of-concept that 6.25 mg ICG was an adequate dose to fluoresce the ipsilateral PNB.

In patients 2 to 5, the first approach was used to identify the PNB. ICG was able to identify the complex of vessels in all patients. ICG was not able to identify the PNB from the mediastinal view. ICG did identify the PNB from the pleural view in 1 patient after the pleura was opened. The PNB distal to the AP window was not visualized in any patient.

In patients 6 to 10, after changing approaches, ICG identified the vessel complex in all cases. The PNB was identified in only one of five mediastinal views but was identified in four of five pleural views (Fig 4). The PNB distal to the AP window was not visualized in any case.

**Comment**

The principles for thymectomy in the management of myasthenia gravis have traditionally included resection of all mediastinal tissue between the 2 phrenic nerves from the base of the diaphragm to the superior poles that course up into the neck region. Therefore, during unilateral RAT, identification of the contralateral phrenic nerve is critical to facilitate complete resection. A reliable and

reproducible method for its identification has not yet been articulated from a unilateral approach. Surgeons have attempted to identify the contralateral phrenic nerve at the origin of the mammary vessels, just distal to the AP window along the mediastinal pleura or by opening the left pleura to directly visualize the nerve from the pleural side. Placement of a contralateral thoracoscope for definitive visualization has been suggested.

Near-infrared fluorescence imaging using ICG potentially offers a more reliable and less time-consuming method for identification of the contralateral phrenic nerve. The major vessels near and around the origin of the contralateral phrenic nerve—the innominate vein, thymic veins, and the internal mammary vessels—were clearly visualized in a chronologic sequence after ICG administration. Most importantly, we were able to trace the left pericardiophrenic vessels down to the left pulmonary hilum intrapleurally while looking into the left chest using a 30-degree scope oriented downward. This identification allowed us to safely preserve the phrenic nerve while extending dissection of the mediastinal perithymic adipose tissue to the area just above this landmark on the left side of the thymus gland.

We were not able to reliably view the PNB from the mediastinal side through the mediastinal adipose tissue with closed or open pleura. This suggests that near-infrared imaging with ICG requires the vessels to not be covered or buried by fatty tissue for identification. Fortunately, the PNB is situated superficially just under the mediastinal pleura on either side, regardless of body mass index. Thus, our current approach to PNB identification includes early identification of the contralateral mammary vessels and then immediate opening of the left pleura widely along the anterior chest wall. We then attempt to visualize the phrenic nerve on the pleural side, and if not readily seen, use ICG to help identify it. Once identified, the pleura alongside the PNB is incised and the mediastinal tissue dissected away from the PNB, preserving its integrity.

We were surprised by the discrepancy in PNB identification between the first approach and the second approach after opening the pleura. The primary difference in approach was the timing of opening the left pleura. We hypothesized that more time elapsed before the pleura was opened in the first approach, giving the carbon dioxide insufflation more time to infiltrate and dissect the pleura along the left PNB. This allows interposed air and carbon dioxide to exist between the left pleura and the left PNB, making the vessels less visible. This is not that dissimilar to operating on a patient with a massive pneumomediastinum, where the air makes visualization of subpleural structures more difficult.

Visualization of the PNB below the AP window remains difficult regardless of whether ICG is used. The PNB falls posteriorly in most patients, and the heart limits any reasonable visualization from a right-sided approach. Proponents of left-sided RAT cite this as a one of the reasons they prefer this side, but the right PNB has a similar course as its loops posteriorly behind the vena cava. In either approach, staying along the edge of the

pericardial fat pad should allow adequate thymic resection and protect the PNB.

In conclusion, near-infrared fluorescence imaging with ICG can be used to identify the contralateral pericardiophrenic vessels and thus the phrenic nerve. This is best accomplished by early identification of the left mammary vessels and opening the pleura widely to view the contralateral PNB from the pleural view in unilateral right RAT. Potentially, this offers a more reliable and less time-consuming method for identification. Further research is required, including whether it reduces operative time.

## Disclosures and Freedom of Investigation

This study was conducted without external funding, and there were no internal sources of funding. The fluorescence camera was purchased as part of the da Vinci system at Swedish Medical Center, and ICG is available from the hospital pharmacy for other applications. Drs. Louie and Farivar receive funds from Intuitive Surgical for speaking engagements and surgical proctorship. Dr Wagner discloses that he had no relationship with Intuitive Surgical at the time of research but as of the acceptance is now employed by Intuitive.

The authors had full control and design of this study, the methods used, the outcome parameters, analysis of data and production of the written report.

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## Disclaimer

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