For more than 15 years, patients with difficult, complicated acute and chronic wounds have come to Ohio State University’s Comprehensive Wound Center. Currently, there are over 12,000 annual patient visits at the center. Recently, we incorporated the LUNA™ Fluorescence Angiography System (Novadaq™ Technologies, Mississauga, Ontario) into our limb salvage program. The use of a fluorescent dye to evaluate blood flow has been utilized by clinicians for over 50 years. Recently, in plastic surgery, surgeons have injected a fluorescent dye called Indocyanine Green (ICG) intraoperatively and, using a special camera, visually observed blood flow to tissue in real time to determine the viability of flaps.

The same technology is now in use to assess the quality of tissue perfusion to determine the viability of tissue in diabetic foot wounds, venous ulcerations, and other non-healing wounds in the lower extremity. Many of these patients will undergo advanced therapies, including hyperbaric oxygen therapy (HBOT) and/or possible wound coverage with either a xenograft or allografts based on determination of local blood flow to the affected area.

In order to gain the best information LUNA can provide and to gain experience with the system for my nursing staff and myself, we have allotted one half-day each week during which we perform LUNA imaging. I have one dedicated nurse who admits the patient to the unit and places the intravenous catheter required for ICG administration. I obtain patient consent for the procedure and perform a complete history and physical. Once this is complete, we are able to proceed with the LUNA imaging studies. Having a dedicated treatment room limits the amount of movement required to operate the machine and allows us to keep all the supplies associated with LUNA imaging in the same area.
Patient positioning is very important in obtaining the best image. It is also important to minimize movement during imaging. If the patient is comfortable and the wound is completely exposed, there will be no secondary movement during the examination. It is essential that 100% of the wound, along with at least 3 cm of unaffected tissue is in the targeted imaging field of view. Bedding, pillows, and clothing should not be in the imaging area. Ambient lighting is used while capturing the initial photograph of the wound, but to acquire the most optimal LUNA images, the room should be dark. We found that using a night-light provides enough illumination to perform the ICG injection, but does not interfere with the visualization of the images on the monitor.

In our current practice, when patients present to the wound center with a chronic lower extremity wound, we typically perform noninvasive vascular studies to assess both arterial and venous flow. In the past, this was limited to ankle brachial index (ABI), venous duplex, transcutaneous oxygen monitoring (TCOM), or photometric plethysmography. All of these examination techniques have limits including when patients present with calcified vessels, which would be non-compressible, leg edema and chronic deep vein thrombosis. None of these examinations allow actual visualization of blood flowing through the vessels nor do they produce images that can be shared in real-time with the patient.

We have just begun to look at a variety of patients with lesions of the lower extremity to determine whether or not LUNA fluorescence angiography could provide valuable information when performed in the outpatient setting. To date, we have imaged about 30 patients who have presented with a variety of lower extremity lesions ranging from chronic osteomyelitis to Wagner stage IV foot ulcers.
Patients presenting to the clinic for fluorescence angiographic evaluation have already been seen and determined to be a good candidate for fluorescence angiography. The only consideration in making this determination is that ICG should be used with caution in patients with a known iodine allergy. We have not sought to pre-medicate these patients at this point. The department of radiology protocol for desensitization for iodine allergy usually requires a hospital stay. It can be administered on an outpatient basis, but the procedure is fairly long in our institution due to repeated doses of prednisone. There is also the possible limitation of intravenous (IV) access. Inability to gain IV access is usually detected during the patient’s initial visit and in some cases, an outpatient PIC line has been ordered to facilitate the LUNA imaging procedure.

Patients typically receive an intravenous dose of 2.5 to 3.0 mL of ICG immediately followed by a brisk 10 mL flush of normal saline for each fluorescence imaging study. Because ICG binds to the plasma proteins in blood, fluorescence angiographic images are visible and recorded within seconds of injection. I routinely capture and record each imaging study over the course of four minutes. The initial blush of fluorescence is followed by the arterial phase and the venous phase of physiologic blood flow. Following image capture, I am able to use the LUNA system’s post-processing analysis tools to objectively analyze the oxygen or perfusion gradient in the wound by placing a perfusion marker indicating dye uptake in the center of the wound and then using subsequent markers at the periwound edge and another marker at least 2.5 cm into normal tissue. This allows us to observe a dye uptake gradient from which you can determine either positive or negative blood flow to the tissue and wound. For example, a diabetic foot wound on the plantar surface of the foot in a patient with monophasic palpable pulses may have an ulcer with 70% dye uptake and a periwound with a 95% dye uptake. This indicates a -25% gradient of hypoxia. This serves as the baseline measurement for the patient, which is important when planning to use HBOT because LUNA imaging can be repeated post-procedure to visually demonstrate whether or not the treatment has resulted in an improvement in perfusion. This would also be important for patients undergoing interventional vascular procedures.

When comparing LUNA imaging to a transcutaneous oxygen-monitoring test in which leads are placed at the level of the knee, superior ankle, and dorsal foot, oxygen level measurements, which are reported in millimeters of mercury, provide a global idea of cutaneous blood flow only. One of the biggest disadvantages of TCOM compared to LUNA imaging is that there is no visual imaging of the wound and periwound.

In the case of patients undergoing HBOT, I have studied them using LUNA at treatment days 0, 10, and 20. The LUNA images have shown that HBOT results in progressive neovascularity, which has allowed us to stop treatments earlier as LUNA images showed due to complete healing. More importantly, patients are able to watch us capture LUNA images and as such, actually become educated to the actual effects HBOT has on their wounds.

Other than the discomfort associated with starting the IV, the LUNA imaging examination is totally painless. Patient tolerances have been 100%. When patients have presented with chronic osteomyelitis of the heel, dorsal foot, and possible ankle lesions, fluorescence angiography demonstrated angiomes and arterial collaterals that have been very helpful to our plastic surgeons in formulating flaps. We are also able to study the vascularity of the postoperative flap should there be a problem. We can better define what constitutes a compromised or failing flap and offer the possibility of HBOT.

**Case study**

A 68-year-old male patient with poorly controlled diabetes was transferred to our wound center from an outside pediatric clinic. The patient had 14 weeks of extensive therapy
including serial debridement, IV antibiotics, and xenograft placement, and was being considered for a fifth toe amputation due to ongoing osteomyelitis. The patient developed a multi-antibiotic-resistant Pseudomonas and his vascular study, which was a non-invasive ABI, was marginal at 0.72.

An ultrasound of the foot revealed ongoing osteomyelitis with a disrupted cortical bone in the metatarsal head of the fifth digit. The ulcer was somewhat clean, but upon debridement, we noted Pseudomonas that was sensitive to ciprofloxacin. The patient had never been offered HBOT for a diabetic foot with osteomyelitis and a Wagner type III ulcer.

We used fluorescence angiography prior to the patient’s first HBOT treatment. At that time, we noted a fairly long, delayed uptake in the ICG dye with the periwound taking up most of the product and the ulcer bed being extremely dusky. We also noticed very little arterial and arteriolar flow and visualization. Most of the foot did not take up more than 50% of the product. The patient had a -60 gradient.

The patient subsequently had HBOT of the diabetic foot at 2.0 ATA, two hours daily, five days per week. He was re-evaluated after his 10th HBOT treatment. The fluorescence angiogram showed dramatic improvement with positive evidence of angiogenesis and neovascularization. There were huge new vessels coming down the ankle and heel into the foot and surrounding ulcer. The distal soft tissue around the ulcer and periwound showed improved dye uptake. The ulcer itself was bright and for the first time, there was good visualization of the fifth toe. The gradient improved to -20.

The patient continued weekly wound care visits with selective debridement and a repeat culture was negative for bacterial growth. The wound itself had improved visually and was starting to show epithelialization.

After his 20th HBOT treatment, there was no longer an observable gradient. The entire foot, including the ulcer, was 100% uniform in the immediate uptake of ICG with no signs of recurrent ischemia. Based on the LUNA imaging evidence, I was able to stop his HBOT treatments. I continued to monitor the patient every two weeks in the wound center and am happy to report that ultimately, we were able to save the foot and avoid amputation.

The patient was able to watch us capture the LUNA imaging studies in real time, ask questions, and be completely involved in his care. He understood the treatment we prescribed and why we chose the HBOT pathway. Viewing the LUNA images increased his involvement in his treatment, encouraged his compliance with the treatment and allowed us to have the positive result.

This patient’s response has been typical of all the patients who have received LUNA fluorescence angiography. The actual real-time visualization of the vascular status of their wounds has allowed our patients to better understand and participate in their prescribed therapy, as well as realistically realize what can and cannot be done. Other noninvasive studies cannot offer this. Patient adherence in this group has increased significantly because of their direct participation during the angiogram.

Several patients who completed their HBOT or surgical therapy with the use of a flap as a result of the information gathered by LUNA imaging, all agree that they were much more confident and comfortable with their treatment than they would have been without actually viewing the test in real time.

**Conclusion**

Fluorescence angiography offers a new dimension in treating lower extremity ulcerations and other chronic non-healing wounds. Not only is the information reproducible and accurate, but it is also supplanting other noninvasive testing by providing real-time visual images of blood flow, which allows patient participation. There have been no complications. It has been well tolerated and if the history and physical are done beforehand, we can eliminate cancellation due to an iodine allergy and make appropriate preparations for intravenous access in a patient with difficult IV issues.

We believe that fluorescence angiography is the best test when dealing with patients with lower extremity wounds and we are continuing to expand indications as we explore the efficacy of fluorescence angiography in the outpatient setting.

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**Reference**


**Suggested Reading**