Use of near-infrared fluorescent imaging with indocyanine green for sentinel lymph node mapping: Preliminary experiences

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Introduction

Precise identification of the most appropriate lymph nodes (LN) for accurate patient staging can be a real challenge in oncologic practice. The gold-standard methods of sentinel lymph node mapping (SLNM) most commonly used in human surgical oncology combine lymphoscintigraphy and operative optical dye, but the combination is not available to the majority of veterinary practitioners. Use of visible blue dyes alone for SLNM has been described, but there are known technical challenges and as a solo technique is considered less accurate than combination methods. An alternative technique of SLNM involves peri-tumoral injection of a fluorescent within the near-infrared (NIR) light spectrum.

The most commonly utilized NIR fluorophore in human and veterinary medicine is the non-targeted agent, indocyanine green (ICG). ICG is highly bound to plasma proteins, making it useful for real-time lymphatic imaging. Direct NIRFL has been described for operative imaging in the clinical treatment of chyllothorax in dogs. Technologies for operative NIR imaging are increasingly clinically available, and use of ICG for indirect near-infrared fluorescent lymphography (NIRFL) for SLNM is increasing in human cancer patients, with excellent correlation to gold-standard SLNM methods.1,2

The aim of this study was to document the initial experiences using NIRFL for SLN mapping in a variety of anatomic locations in dogs with naturally-occurring neoplasms prone to lymphatic metastatic patterns.

Materials and Methods

Retrospective multi-institutional case series with data collected from the medical records of clinical patients. Dogs with naturally-occurring solid tumors that underwent operative SLNM using indirect NIRFL with ICG were included. Data is descriptively reported as median (range).

Results

29 client-owned dogs (age=10.4 (5.6-13.4) years, body weight=28.5 (13.3-63.5) kg) with 30 distinct tumors (carcinomas (n=15); pulmonary=5, anal sac=5, thyroid=5, pyloric gland (n=13), and oral melanomas (n=2)) were included, with a total of 46 SLNs removed. NIRFL was performed by to-effect peri-tumoral injection of 0.4-2.0 ml of 0.25 mg/ml ICG in a 4-quadrant technique followed by peri-tumoral massage, using one of 2 imaging systems: The miniFLARE open NIR imaging system (Fig. 1-3) or the Storz D-light rigid endoscopic NIR imaging system.2 Regional locations of primary tumors included intrathoracic (5), head/neck (10), trunk (4), perineum (5), and extremity (6), with SLNs subsequently identified as tracheobronchial (5), mandibular (5), mediastinal (5), iliac (2), popliteal (5), inguinal (4), and superficial cervical (2).3

Successful identification of at least 1 SLN by NIRFL was achieved in 93% (28/30) of tumors studied; LN fluorescence commonly occurred ≤1 minute. Subjectively superficial lymphatic pathways could be tracked transdermally with NIRFL but were more easily lost in deeper tissues. NIRFL identified ≥2 SNL by distinct lymphatic pathways in 40% (12/28) of tumors (pathways could be visualized as distinct). Clear positive correlation of identified SLN with expected SNL occurred in 39% (11/28) of tumors, but the expected SNL was incorrect (Figure 4) or incomplete (e.g., more than 1 SLN identified) in 61% (17/28 tumors). Lymphatic metastasis was identified histologically in 52% (13/25) of SLNs that exhibited fluorescence and were removed. In 14% (3/21) of tumors with ≥2 SNL, only 1 of the multiple SNLs identified was positive for metastasis. Tumor locations that failed NIRFL or provided technical challenges in NIRFL or LN removal: Thyroid (3/5), Lung (3/5), Trunk (2/4), Anal Sac (5/5), Limb (6/6), Head/0/5). SLN removal was not performed due to NIRFL or operative technical challenges in 25% (7/28) tumors. No NIRFL-related complications were identified.

Discussion

Initial experience demonstrates that NIRFL can be safely and successfully used for SLNM procedures in a variety of anatomic locations. Metastatic disease was identified in a high proportion of SLNs identified in this mixed tumor-type cohort, supporting the continued investigation of disease-and species-specific application of SLNM. While good evidence exists in humans that NIRFL has similar SLNM accuracy to combination methods,3 this study is limited to no comparison with gold standard was used to verify accurate identification of all SNLs, which may have resulted in missed SNLs or precise LN misidentifications in certain locations. Comparative SLNM technique studies would be useful.

While overall very promising, technical challenges do exist for NIRFL SLNM. Canine lymphocenter anatomy (fewer, proportionally larger LNs, located further apart anatomically) differs from humans, which may impact the application of NIRFL as a solitary method of SLNM in dogs compared to results obtained in humans. ICG transit through afferent and efferent lymphatics is rapid and timing of injection is important to avoid missing the correct LN or prevent incorrect diagnosis of 2 or 3 LNs as sentinel. Even in humans, technical aspects of SLNM are often poorly standardized; this is definitely lacking for canine patients, which will be important in interpretation of future disease-specific metastatic data, especially in low volume cohorts. To ensure all SLNs are identified and to improve procedural positioning, combination of operative NIRFL with preoperative SLNM4 in certain patient subsets may optimize application of SLNM. Numerous patient, surgeon, and technical factors can impact the application and interpretation of results with different SLNM techniques, and further prospective study of NIRFL in veterinary patients is recommended.

References


Figure 1: Fluorescent lymphatic vessels viewed transdermally along the medial thigh, running proximally to emerge on the inguinal LN. A small incision allows visualization of the inguinal LN and demonstrated fluorescence from ICG uptake identifies it as the SLN (yellow arrow).

Figure 2: View of medial thigh. Continuing to follow lymphatic vessels (yellow arrow) transdermally along medial thigh toward the region of the inguinal LN (yellow X) via visualization with NIR imaging.

Figure 3: Fluorescent lymphatic vessels viewed transdermally along the medial thigh, running proximally to converge on the inguinal LN. A small incision allows visualization of the inguinal LN and demonstrated fluorescence from ICG uptake identifies it as the SLN (yellow arrow).