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LYMPHOSCINTIGRAPHY

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ABSTRACT

Lymphoscintigraphy is rapidly gaining favor as a noninvasive technique to assess lymphatic structure and function. The following essay summarizes the historical background and provides a synopsis of personal experience with radiolabeled (99mTc) human serum albumin (HSA) using this technique.

HISTORICAL

The flow of lymph throughout the body was mapped by Sappey (1) through meticulous dissection. After the discovery of x-ray techniques, contrast lymphangiography was developed but the procedure is time-consuming and requires incision to gain access to lymphatic channels.

The discipline of nuclear medicine discloses physiology and pathophysiology using radioactive tracers. One physiological process commonly studied is transport, where a tracer is injected at one site and then followed with a detector to record the rate and direction of movement of the radiolabeled agent. This method was first examined in the blood vascular system but early workers in nuclear medicine also reported regional lymph node migration of subcutaneously injected tracers (2). During the 40 years since this was first seen, lymphoscintigraphy (LSG) has evolved into a useful procedure.

TECHNIQUES

Early studies utilized colloidal Au-198 for pelvic carcinoma, showing paraaortic drainage patterns (3) and for breast carcinoma, showing axillary and parasternal drainage (4) with the best imaging of nodes with Au-198 scans first reported between 1965-1969 (5). Gamma cameras came into general use in the 1970s. Whereas these cameras are now usually computer-equipped and allow dynamic quantitation, they have required new tracer agents as will be described.

Ege (6) introduced internal mammary lymphoscintigraphy and has used this technique successfully in many thousands of patients (7) to the point that the procedure has been endorsed as standard practice for breast tumor staging by some surgeons (8). General acceptance, however, is far from universal.

Iliopelvic lymphoscintigraphy was also first described by Ege (9) and more recently reviewed by Kaplan (10). Perianal injections of antimony colloid are followed by delayed images after 3-6 hours. Prostatic carcinoma has been studied by direct injection of colloid into the prostate (11).

Modern equipment which permits computerized data acquisition with contrast enhancement and quantitation of images is now desirable for lymphoscintigraphy. This approach is especially true for studies in benign diseases (12) recently amplified with Tc-99m human serum albumin (HSA) (13). In the case of lymphedema, Tc-99m antimony colloid has been used successfully, although studies are usually prolonged for several hours.

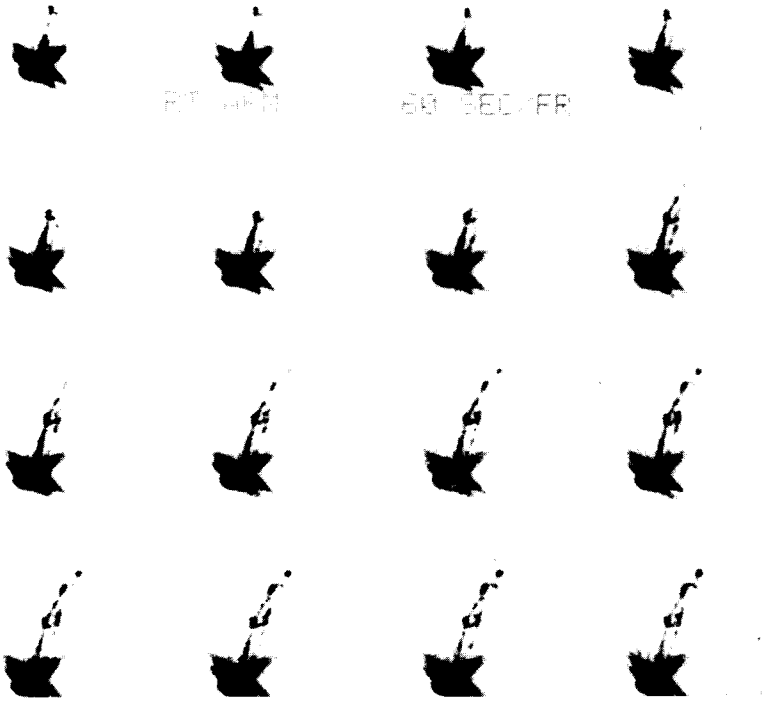

Fig. 1. Serial one-minute images (each frame left to right) of right arm after injection of Tc-99m human serum albumin (HSA) intradermally around forearm melanoma. Early paradeltoid uptake was found to represent pigmented node. Axillary uptake is seen from six minutes post-injection onward.

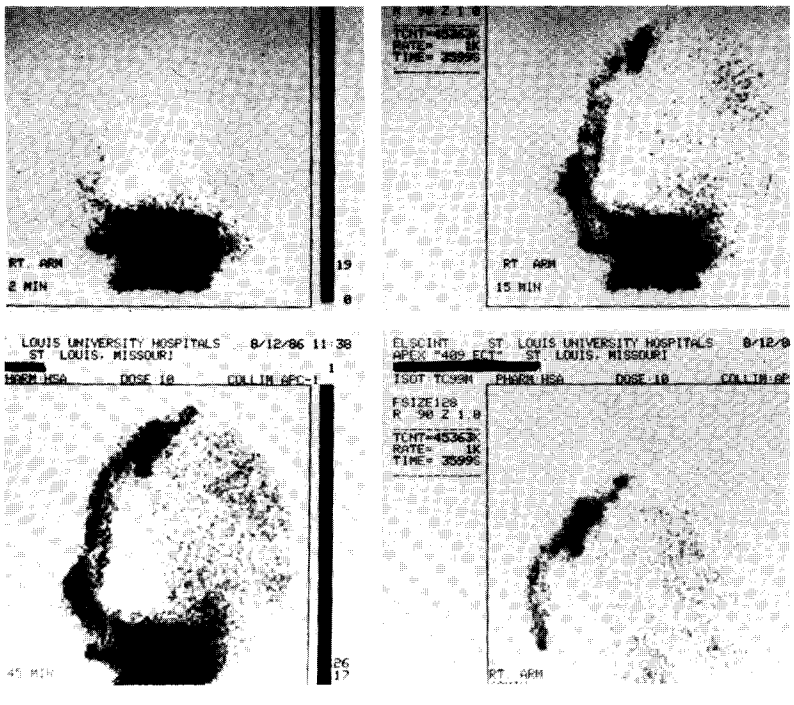

Fig. 2. Lymphoscintigraphy images 2-60 minutes after injection of forearm melanoma: note early epitrochlear node uptake, axillary nodes at 15 minutes, and supraclavicular nodes at 45 minutes but minimal systemic background by 60 minutes.

MATERIALS

Colloidal Au-198 was utilized during early studies, but its long half-life and energetic emission prohibits its use by current standards.

Colloid labeled with technetium (Tc-99m), a versatile, short-lived radionuclide with ideal gamma photon energy for gamma camera imaging, has been standard since the early 1970s. Different sizes and types of colloids have been compared (14). The governing principle is that the smaller the colloid the better the migration through lymphatic vessels after interstitial injection. A colloid of antimony sulfide (15,16) has achieved widest use, although it has not yet been released for routine imaging studies in the United States. Antimony sulfide (Cadema Medical Products, Middleton, NY is sole supplier in the U.S.) has a particle size of 3-12mm, about the same as colloidal gold, and this feature combines desirable physical characteristics with ease in handling (Lieberman, E. personal communication). Other colloids which have been utilized include stannous phytate, found to be inferior to antimony sulfide (15); rhenium sulfur colloid (17), an albumin microcolloid, Dextran (18) and human serum albumin (HSA) (19). The latter two are not colloids per se, but macromolecules that migrate through the lymphatic system in a similar pattern to colloids. In our laboratory at St. Louis University we have recently used Tc-99m HSA for dynamic lymphoscintigraphy which allows quantification of both flow rates and patterns of migration.

CLINICAL UTILITY

Malignant Melanoma

The most universally accepted use of LSG is probably in the management of malignant melanoma (20). In Logic's series of 105 patients with truncal melanoma, over 50% had lymphatic drainage which crossed over the midline and/or Sappey's line (21). This finding agrees with the smaller series of Sullivan et al (21), Wanebo et al (22), and with our own experience using both Tc-99m antimony colloid and Tc-99m HSA. We prefer the latter agent because it permits dynamic and quantitative information on lymphatic drainage and in-transit lymph nodes along these pathways. We are finding LSG just as important in management where expected lymph drainage does *not* occur and no enlarged lymph nodes are palpable. Together these findings signify that tumor spread to the regional nodes in question is unlikely. This conclusion is probably invalid for deep nodes where clinical assessment by palpation is not possible. If dynamic LSG is interpreted in terms of probability, it serves a far better function in delineating the likelihood of tumor involvement then attempts to infer whether nodes are replaced by metastases from nodal configuration on delayed scans alone.

Figures 1-5 illustrate selected experience with dynamic LSG using Tc-99m HSA.

Breast Carcinoma

Ege (6,7) has studied over 5,000 patients with internal mammary LSG and more recently has reviewed adding axillary LSG to the internal mammary LSG (23). Whereas axillary LSG is "at least as accurate as clinical assessment" it cannot as yet replace pathologic examination of regional nodes for optimal staging (23). The most valuable aspect of LSG in staging breast carcinoma is the internal mammary approach, injecting into the posterior rectus sheath bilaterally. In 981 breast carcinoma patients without axillary metastases there was a two- to three-fold increased recurrence rate associated with abnormal LSG, suggesting that patients with these findings require more vigorous adjuvant therapy (24).

Pelvic Tumors

Iliopelvic LSG has not gained widespread acceptance, either because of poor technique or misunderstanding of the procedure. Dynamic LSG, as for example, with Tc-99m HSA may become especially useful here (25).

Lymphedema

Quantitative studies of lymphatic flow in lymphedema (13) are beginning to be ap-

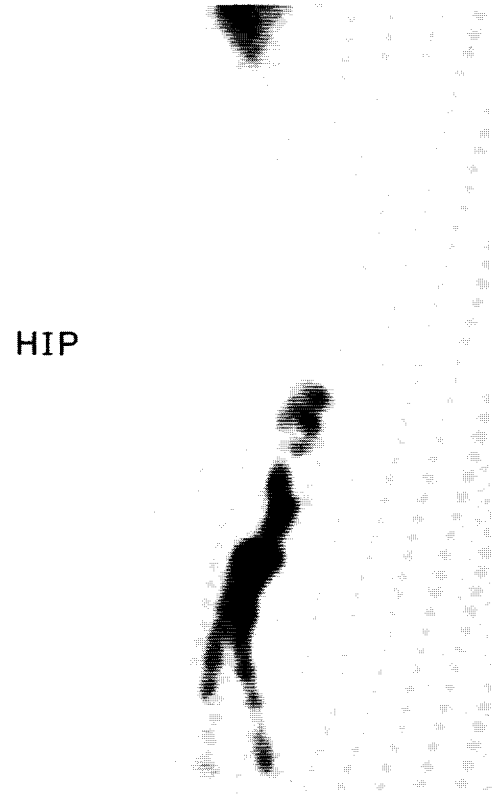

Fig. 3. Lymphoscintigraphy image 15 minutes after injection of ankle melanoma. Prominent inguinal node uptake is apparent.

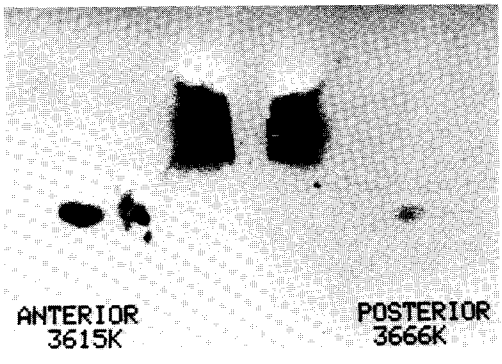

Fig. 4. Anterior and posterior lymphoscintigraphy 60 minutes after injection around melanoma of left buttock. Left inguinal uptake is seen, plus urinary bladder activity (left side) and faint visualization of intergluteal node (right side).

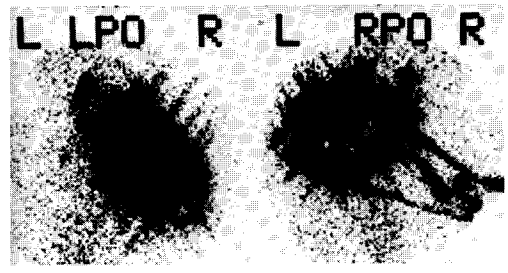

Fig. 5. Lymphoscintigraphy 60 minutes after injection around skin graft at site of melanoma in left upper thorax. There are multiple channels to the right axilla (R) but no visible drainage to the left axilla (L). LPO-left posterior oblique; RPO-right posterior oblique.

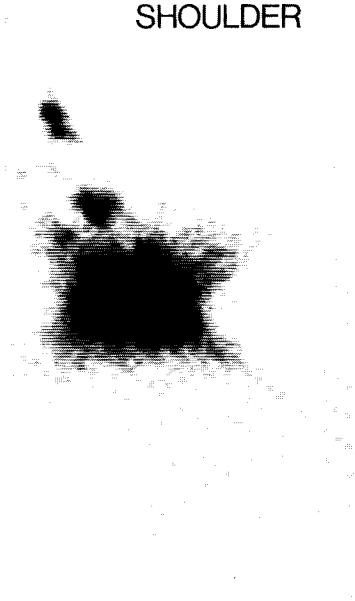

Fig. 6. Lymphoscintigraphy of male patient with melanoma anterolateral to left nipple. There is prominent supraclavicular and anterior cervical drainage but no axillary visualization. The faint starburst artifact arises from residual activity at the injection site.

preciated and may be expected to evolve as a procedure useful to both lymphologic research and clinical management. For example, a ten- to twenty-fold increase in lymphatic flow with infection has been estimated using LSG (13).

PROSPECTS

Abdominal LSG as a replacement for contrast x-ray lymphography is undergoing intensive study (25), and LSG may soon replace contrast angiography in evaluation of lymphedema (13). The limiting factor in LSG is often the placement of the radionuclide in the exact location to visualize the lymphatic drainage system of interest, and accordingly, is more difficult with deep structures than with skin. As it becomes more generally recognized that interpretation of nodal involvement with tumor using contrast lymphography is often inconclusive (26), probability of metastases based on dynamic LSG is likely to become more widely utilized. "At the very least, the techniques used for radiocolloid LSG permit improved understanding of lymphatic system function" (26).

The altered dynamics of lymphatic flow following surgery have led to some confusion but LSG has been useful in evaluating reconstructive operations involving transplantation of lymphatics (27). Further work along these lines is expected.

A whole new era is now upon nuclear medicine with monoclonal antibody imaging undergoing development for several diagnostic and therapeutic uses, included among them human melanoma (28) and visceral tumors. The limiting factors of specificity/nonspecificity and of radiochemical inactivation of highly labeled antibodies are currently being explored.

LSG has become an integral part of nuclear medicine. Either Tc-99m antimony sulfide or the new Tc-99m HSA is providing valuable new insight into both lymphatic structure and (patho)physiology.

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