LYMPHOSCINTIGRAPHY IN THE DETECTION OF SENTINEL LYMPH NODES

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LYMPHOSCINTIGRAPHY

Background
In the 1970's, Ege [1977, 1983] used subcostal injections of radiocolloid to determine the status of the internal mammary chain in patients with carcinoma of the breast. The radiocolloids traveled via lymphatic channels to nodes where fixed macrophages in the reticular endothelial system engulfed the colloid. Her work was the first to utilize lymphoscintigraphy in a large scale for breast cancer evaluation. The internal mammary nodes with tumor showed decreased or absent activity, and at times, diversion of tracer to the contralateral side because of obstructed lymphatics. While this technique has not been used in recent years it marked the advent of lymphoscintigraphy in patients with breast cancer.

More recently, the concept of the sentinel lymph node (SLN) has developed. The SLN is defined as the first metastatic node. Morton and his colleagues [Morton 1992a, 1992b, 1997a, 1997b, 1999a] were the first to use blue dye and later, radiotracers to locate the SLN in patients with malignant melanoma. The Delphian node in thyroid cancer has been noted in textbooks for years [DeGroot 1996, Daniels 1991]. In 1960, Gould [1960] used the term, “sentinel node”, as a commonly positioned node in patients with parotid carcinomas. Cabanas [1977] studied 100 patients with radiographic contrast to determine, what he also, independently described as the sentinel node. He makes no mention of the work by Gould in his references. Cabanas found that in patients with penile cancers; the sentinel nodes could be evaluated with contrast lymphangiography. He also found that patients with negative sentinel node biopsies and negative dissections had the best prognoses. Those with a positive sentinel node and no other involved nodes had slightly worse prognoses, while the patients with positive sentinel nodes and additional positive nodes on completions lymph node dissection had the worst prognoses. His work did not receive acceptance. Wong, Cagle and Morton [1991] used blue dye in a cat model to determine its effectiveness in locating the SLN. Cabanas is not mentioned in their original paper. In 1991, Morton [1992b] used lymphoscintigraphy to determine sentinel node activity. Morton and his colleagues are to be acknowledged for developing the concept of the sentinel node. Eventually, radiotracers were used to find the sentinel node. Krag [1995, 1998], Reingten [1997, 1998a, 1998b] and Giuliano [1994] further promulgated the concept. These groups helped develop the sentinel lymphadenectomy as common practice in oncologic surgery in melanoma and breast cancer. The SLN has been defined in patients using blue dye, radioactive colloids, or both.
The early investigators such as Grant [1959], Turner-Warrick [1953] and Vendrell-Torne [1972] were instrumental in developing the pathophysiology of lymphatic drainage of the breast.

THE TECHNICAL ASPECTS OF LYMPHOSCINTIGRAPHY

Radiopharmaceuticals
Historically, the first tracer used for lymphoscintigraphy was radioactive Gold 198 (Au 198) [Kazem 1968]. The study by Vendrell-Torne [1972] showed migration of tracer after intraparenchymal injections to the axillary and internal mammary nodes. The particles of Au 198 were quite small, similar to the particle size of Antimony sulfide colloid [Uren 1995, DeCicco 1997]. In the study by Vendrell-Torne [1972], patients were put into five groups, receiving injections into either one of the four quadrants of the breast or into the periareolar area. Virtually all patients had drainage into the axillary chain, regardless of the site of injection. With an upper inner quadrant injection, 80% of the patients were found to have uptake into nodes of the internal mammary chain. The outer quadrants had less activity entering the internal mammary chain. Even by the poor imaging characteristics of rectilinear scanning, they were able to find intramammary nodes. Rectilinear scanning is no longer used to any extent in Nuclear Medicine.

The agent that is most available in the United States is Technetium99m Sulfur Colloid made by the thiosulfate method [Kowalsky 1987, Eshima 1996, Glass 1998]. Technetium 99m (Tc99m) is the radioactive atom that is used to tag the colloid lymphoscintigraphy. Tc99m is an ideal agent for imaging and counting because of its physical half-life, ease in compounding and relatively low dose to the patient as well as individuals caring for the patient. Its further benefit is that it gives minimal particulate energy from internal conversion electrons of low abundance of 10 %. In the process of decaying, it gives off a gamma photon of 140 keV. Because of relatively smaller amounts of energy absorbed in tissue, radiation to the patient is lower compared to other tracers such as I-131 which has significant more amount of particulate energy. Tc99m has a physical half-life of 6 hours. Tc99m is the most common tracer used in Nuclear Medicine since it can be complexed to a myriad of compounds such radiopharmaceuticals for the heart, bone and kidney. In lymphoscintigraphy, relatively small doses are given in the range of several hundred microcuries to a millicurie. In other studies in Nuclear Medicine, such as the heart studies, typical doses are in the range of 20 to 25 mCis.

Tc99m is made in a vial where H₂S is created with the resultant formation of a large number of different size colloidal sulfur particles. To obtain more uniformly sized particles, the tracer is filtered through a .22-micron filter, which removes particles whose size is larger than 220 nanometers (nm). A direct method of making Tc99m sulfur colloid can be made from using H2S gas. H2S is highly toxic and requires the use of well-ventilated and isolated fume hood. Particles made by this method have particles in the range of those of antimony colloid.

Other tracers that are available in Europe and Australia include Tc99m antimony colloid and Tc99m albumin minicolloid [De Cicco 1997, Uren 1995]. Tc99m mini albumin colloid is no longer available in the United States. Tc99m albumin (not colloidal) is available in the United States and passes through