

This Week's Citation Classic

Wagner H N, Jr., Sabiston D C, Jr., McAfee J G, Tow D & Stern H S. Diagnosis of massive pulmonary embolism in man by radioisotope scanning. *N. Eng. J. Med.* 271:376-84, 1964. [Depts. Medicine, Surgery, and Radiology, Johns Hopkins Univ. Sch. Med., Baltimore, MD]

In this paper, we described the development and application of the use of radioiodine labeled macroaggregates of albumin in the diagnosis of acute pulmonary embolism. [The SC® indicates that this paper has been cited over 245 times since 1964.]

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"The research described in this paper is an illustration of how progress often depends on the existence of a problem. As cardiac surgery expanded in the early 1960s, attempts were made to treat patients with massive pulmonary embolism and circulatory collapse by removal of the clots from the occluded pulmonary arteries, first without, and subsequently with, cardiopulmonary bypass. This necessitated a diagnostic technique that would permit accurate diagnosis rapidly since the patients were critically ill. Pulmonary angiography was in the process of development, but was time-consuming and not widely available.

"At the same time at Johns Hopkins and in a few other institutions, research was being conducted on the use of aggregated human serum albumin to study the phagocytic process of the reticuloendothelial system. Such particles were injected intravenously and were removed by the liver and spleen where the accumulation of the radioiodine label could

be imaged with the developing rectilinear scanners. These were beginning to be used to visualize organs and lesions that could not be seen with x-radiographic techniques. The albumin aggregates were prepared by heating human serum albumin under carefully controlled conditions. At times when heating was excessive, the particles became too large to pass through the pulmonary capillary bed. These could be observed to be distributed throughout the lung and it could be shown in animals that they did not enter the region of reduced pulmonary arterial blood flow associated with embolism. The first studies were a series of 42 dogs with experimentally produced emboli in which the correlation of the site of the lesions with the perfusion defects in the scans was good. The next step was to carry out toxicity studies in animals. These showed that the hemodynamic effects were negligible and the particles were not antigenic.

"The first lung scan was performed on me in September of 1963. Masahiro Iio, a research fellow and now a leading nuclear physician, injected the macroaggregates (we called them this to distinguish them from the smaller particles used to study the reticuloendothelial system), and James Langan, now our chief technologist (then our only nuclear technologist), performed the scan. The first patient with pulmonary embolism was a 75-year-old woman with a mid thigh amputation and shock who was operated upon by David Sabiston at Johns Hopkins in October, 1963. The series of patients we studied subsequently formed the basis of the report.

"I think one reason for my publication being highly cited is the fact that prior to the development of a single diagnostic test pulmonary embolism was a diagnosis usually made only at autopsy."