

# This Week's Citation Classic®

Higashi T, Nakayama Y, Murata A, Nakamura K, Sugiyama M, Kawaguchi T & Suzuki S. Clinical evaluation of  $^{67}\text{Ga}$ -citrate scanning.

*J. Nucl. Med.* 13:196-201, 1972.

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Gallium-67( $^{67}\text{Ga}$ )-citrate scintiscans was performed in 149 cases with a variety of malignant, benign, and inflammatory lesions.  $^{67}\text{Ga}$ -citrate was noted to be valuable in the diagnosis of cancers of the lung, the breast, and the maxillary sinuses. [The *SCI*® indicates that this paper has been cited in over 180 publications.]

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For a long time, numerous investigators dreamed of using radioisotopes to delineate a malignant tumor as a positive image. However, radiopharmaceuticals clinically sufficient for tumor detection had not yet appeared.

The first suggestion, in 1969, that gallium-67( $^{67}\text{Ga}$ )-citrate might localize in tumors was based on a serendipitous finding by C.L. Edwards and R.L. Hayes.<sup>1</sup> Although nearly 20 years have elapsed since their findings,  $^{67}\text{Ga}$ -citrate is still widely used to diagnose malignant tumors and inflammatory lesions.<sup>2,3</sup>

In 1969 Philips Duphar Cyclotron and Isotope Laboratory in The Netherlands was first to supply us with  $^{67}\text{Ga}$ -citrate. In our laboratory, however, we noticed a white precipitate floating in a sample bottle given to us. We postulated that this floating precipitate was produced by alteration of the pH of the liquid. Needless to say, it was impossible for us to use this for *in vivo* experimentation. Some hospitals that were also supplied with the same sample of  $^{67}\text{Ga}$ -citrate were forced to give up

using it clinically. We, however, filtered the opaque liquid using a Millipore filter and then cautiously injected it into a patient with squamous cell carcinoma of the lung. We succeeded in obtaining a clear and strong positive image corresponding to an abnormal shadow on a chest X ray.

I still vividly remember this beautiful positive image and even now cannot wipe its image from my mind. Subsequently,  $^{67}\text{Ga}$  scanning was performed on many cases of malignant, benign, and inflammatory lesions in cooperation with Yokohama Keiyu Hospital in Japan and, in 1972, our clinical results were published in this classic paper. It is probably highly cited because we evaluated, clinically,  $^{67}\text{Ga}$ -citrate scanning of various lesions and organs of many patients and obtained good results at an early stage in its use. This study is a useful reference for doctors studying Ga scanning in detail.

In addition, in 1971 we were the first to discover how iron administration affects the distribution of  $^{67}\text{Ga}$ -citrate in human tissues.<sup>4</sup> We determined that Ga is closely related to iron metabolism since Ga is a Group IIIb metal that resembles the ferric ion. (Iron is an important element for cellular metabolism and proliferation.)

Consequently, we suggest that there is correlation between the uptake of  $^{67}\text{Ga}$ -citrate and the rate of cellular proliferation in malignant tumor cells. The uptake of  $^{67}\text{Ga}$ -citrate in malignant tumor cells may be correlated with sensitivity for treatment and prognosis.<sup>5,6</sup>

Recently, research in immunodetection of cancer has been performed by numerous investigators throughout the world.  $^{67}\text{Ga}$ -citrate is not specific for malignant tumor cells, and it is an uncomplicated diagnostic procedure readily available for clinical use. Thus,  $^{67}\text{Ga}$ -citrate could be used widely on a clinical basis in many hospitals to detect malignant tumors and inflammatory lesions.

1. Edwards C L & Hayes R L. Tumor scanning with  $^{67}\text{Ga}$  citrate. *J. Nucl. Med.* 10:103-5, 1969. (Cited 435 times.)

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3. Bekerman C, Hoffer P B & Bitran J D. The role of Ga-67 in the clinical evaluation of cancer.

*Semin. Nucl. Med.* 15:72-103, 1985.

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