

# Icg Versus 99tc in Breast Surgery-How to Match Quality Health Care and Costs Reduction: A Cost Effectiveness Study

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## Abstract

**Introduction:** Scientific evidence shows how ICG sensibility and specificity is comparable to 99Tc, and in many Breast Units ICG has become the gold standard for sentinel lymph node detection. Aim of this study is a cost-effectiveness analysis of the sentinel lymph node detection pathway using ICG, compared to the 99Tc one.

**Materials and methods:** 291 patients received a 99Tc injection the day before surgery and an ICG one in the OP day. As in our hospital a Nuclear Medicine Department does not exist, patients had to undergo an adjunctive travel in order to receive Technetium. We calculated costs of the whole Technetium procedure as like as the costs of the ICG one.

**Results:** The overall amount of costs of the Technetium injection has been equal to 450363,62€. The ICG pathway has had an overall cost of 98668,7€, equal to a 21.9% of the Technetium expenses.

**Discussion:** According to the Law, Technetium may be managed only in a Nuclear medicine department. This is the reason why Patients undergo a sometimes long travel to reach one. This traffic represents a cost for Patients and a work overload for the hospital structures. Indocyanine green allows to avoid a travel to the Nuclear Medicine and to spare a big amount of costs.

**Keywords:** Lymph node; Breast surgery; Nuclear medicine; Cost reduction

## Introduction

Sentinel lymph node detection and analysis is nowadays a widespread and consolidated technique to find a possible nodal breast cancer involvement. A lymph node metastasis is nowadays enough to give indication for a complete axillary dissection [1-3].

The first node draining the breast tissue is named "sentinel", as it is the first nodal station draining lymph coming from the neoplasm. In case of a cancer free sentinel node, it is assumed that all the other axillary nodes should be disease free, too. A diseased node, on the contrary, may not exclude an involvement of any other axillary node, and then a complete axillary dissection is often needed [1].

There are no macroscopic parameters to determine whether a node is the "sentinel" one or not. This considered, a sensible and specific detection method is absolutely crucial. Many possible methods have been suggested in the past: in the last years, the gold standard has been a radioactive tracer injection, 99Technetium [4], which is able to follow the lymphatic stream up to the first node. Technetium in the node may be easily detected using a Geiger counter (Gamma Finder), allowing then to recognize the right sentinel lymph node.

Technetium as a tracer entails some difficult management aspects. As a radioactive material [5], a Technetium injection can be performed only in a Nuclear Medicine Department. Thus, all the breast surgery patients must, as outpatients, travel to this structure before the operation, generally one day before or in the same surgery day, to receive the tracer. Moreover, Technetium itself is a possible source of pollution, due to its urinary clearance, and may determine a possible radioactive exposure for patients' relatives, hospital workers and the whole environment [6-9] (Technetium has a 6.1 hours half-life). All the injected patients must remain some hours in hospital for clinical observations to reduce this risk.

In the end, not all the hospitals are provided with a Nuclear Medicine Department, big hospitals may be often not provided as well. Then, patients' enrolment is often difficult, and eventually requires two travels: one to the Nuclear Medicine, one to the surgical unit.

In the last 3 years, an alternative detecting method based on a biologic stain called Indocyanine Green (ICG) has been introduced and validated [10-12]. This is a non-radioactive stain used nowadays for many medical purposes, including the study of blood perfusion through an intravenous injection [13] and the liver function assessment through the measure of its clearance during transplantative surgery [14].

ICG is useful in sentinel lymph node surgery due to its fluorescence in infrared spectrum. Its use requires a periareolar intraoperative injection and the observation of the surgical field through an infrared camera [10]. ICG migrates through the lymphatic vessels to the axilla and, as it is much more fluid in comparison with Technetium, its migration to the axillary lymph nodes is a matter of minutes, mostly 6 or 7. This is the reason why the whole procedure can be performed directly in the operatory room, at the beginning of surgery. The enlightened lymph node, collecting ICG, is the sentinel one, ready to be removed and analyzed.

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**Received** October 28, 2016; **Accepted** February 18, 2017; **Published** February 26, 2017

**Citation:** Cattin F, Fogacci T, Frisoni G, Fabiocchi L, Dellachiesa L, et al. (2017) Icg Versus 99tc in Breast Surgery-How to Match Quality Health Care and Costs Reduction: A Cost Effectiveness Study. J Cancer Sci Ther 9: 340-342. doi: 10.4172/1948-5956.1000439

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Scientific evidence shows nowadays how ICG sensibility and specificity is comparable to 99Tc [11,12]. Thus, in many Breast Units ICG has become the gold standard for sentinel lymph node detection. Among these centres stands the Breast Unit of the Santarcangelo di Romagna hospital, where, after two years of an experimental combined ICG and 99Tc use, since last year ICG has become the only tracer used in breast surgery.

Aim of this study is a cost-effectiveness analysis of the sentinel lymph node detection pathway using ICG, compared to the 99Tc one.

## Materials and Methods

In the period, January 2013-July 2014, in the Breast Unit of the Santarcangelo di Romagna hospital a non-superiority study of ICG versus 99Tc has been carried out. During this period, 291 Patients were selected and underwent a breast surgery requiring a sentinel lymph node detection. All of these patients received a 99Tc injection prior to surgery, as like as an ICG one directly in the operatory room.

As the Santarcangelo hospital does not include a Nuclear Medicine Department, its Breast Unit needs, for a Technetium injection, the nearest one, which is in the "Bufalini" hospital, in Cesena.

To prepare our analysis, we have compared the cost-effectiveness of the two pathways using the same patients, in order to avoid any possible selection bias.

As said, Technetium requires two travels: the first one to reach the Nuclear Medicine Department, the second one (normally the day after) to the Surgical Department for surgery. To ascertain the cost of these travels, we have considered each Patient's residency and the distance (in kilometres) to and from the Cesena hospital and the Santarcangelo one (source: [www.viamichelin.it](http://www.viamichelin.it)). The ICG tracer does not require a travel to a Nuclear Medicine, then we have considered the distance just to the Santarcangelo hospital.

The refund parameters determined by the Health System Organization "AUSL Romagna" have been useful to determine the costs of each travel. Even if it is clear that Patients' travels may not receive any refund, as breast cancer is not included in the refundable diseases' list, data are useful indeed to have a glance of costs. The amount of refund per kilometre is equal to 1/5 of petrol cost per litre, determined every first day of the month. At the study time (October 2015) the refund amount is equal to 0.2788€ per kilometre.

We analyzed the cost of the two clinical pathways. It appeared that the Technetium one requires an average of 100€ per each drug dose, 700€ of medical/nurse expenses and 700€ of hospital expenses (clinical observation in bed for 5-6 hours). This means a whole amount of 1500€ for each Patient (source: SEDA Ltd, Trezzano sul Naviglio, Milan, Italy).

Each bottle of ICG has a cost of 70€, and is enough for 4 procedures. ICG requires a non-reusable kit as well, which costs 85€. A dedicated fluorescence detecting camera is required as well, and it costs 50000€. Its depreciation has been arbitrarily distributed over the first 250 Patients (200€ each. Source: SEDA Ltd., Trezzano sul Naviglio, Milan, Italy).

99Tc does not interfere with the duration of surgery. ICG makes surgery an average of 4-6 minutes longer (the time required by ICG itself to reach the sentinel lymph node). This is the reason why the slightly enhanced costs of the surgical procedure have been considered as irrelevant.

## Results

If we consider all the reported parameters, it derives that the 291 Patients, when using Technetium as a tracer to detect a sentinel lymph node, would have travelled a whole of 49778.5 Km (Home-Cesena hospital and back, home-Santarcangelo hospital and back). On the contrary, the same 291 Patients, using ICG as a tracer, would have travelled a whole of 18861,7 Km (Home-Santarcangelo hospital and back).

When we consider the overall amount of costs of the Technetium injection, including all the considered parameters, it has been equal to 450363,62€. The ICG pathway for the same patients, has had an overall cost of 98668.7€, comprehensive of the detecting camera depreciation, equal to a 21.9% of the Technetium expenses (Table 1).

## Discussion

To our knowledge, this is the first cost-effectiveness study comparing a traditional and established way to detect an axillary sentinel lymph node and the Indocyanine Green method. The latter has been proposed at the beginning of the 10th of the XXI century, and is based on a biologic tracer known since the fifties. Indocyanine green is nowadays used for traditional purposes (organ perfusion and liver function) as like as for sentinel lymph node detection in several organs, among which stomach, bowel, vulva and breast are to be mentioned [10-16].

The breast sentinel lymph node detection through ICG consists in the tracer injection and then in the lymph node detection through an infrared camera. ICG infrared emission stands in the first transparency window for soft tissues both for the maximum absorption peak (778 nm) and for the maximum emission one (830 nm). This is the reason why the camera uses a 778 nm infrared LED light source, and detects a 830 nm emission reply. This limits as much as possible interferences coming from other structures [15]. Once injected in the operatory field, generally under the areola, ICG shows the lymphatic vessel course up to the first draining lymph node. This lymph node can be, then, taken as a specimen and analyzed as the sentinel one. This is the reason why ICG requires neither a Patient's preadmission, nor any hospitalization except for surgery. ICG shows a fast transfer to the axilla, normally within 10 minutes, and this makes the time elongation of surgery irrelevant.

On the other side, the traditional sentinel lymph node detection using 99Tc requires a hospitalization in a Nuclear Medicine Department-generally the day before surgery-for tracer injection. Technetium is then detected in the surgical field using a Geiger counter (Gamma Finder). This is the reason why a cost-effectiveness analysis of this pathway needs to consider the preadmission and clinical observation costs as like as the medical and injection ones.

	99Tc	ICG
Travelled kilometres (total)	49778.5	18861.7
Cost for patients (travel) (€)	13863.62	5249.39
Cost of Medium of Contrast (€)	29100	5092
Cost of non-reusable materials (€)	0	24735
Medical/Nurses costs (€)	203700	Included in OR costs
Hospital structure costs (€)	203700	Included in OR costs
Cost of dedicated camera (€)	0	50000
Cost of the clinical pathway (€)	436500	79827
Whole cost (€)	450363.62	98668.7

Table 1: All the considered parameters, it has been equal to 450363,62€.

Considering data in the Literature, showing an equivalence in sensibility and specificity between the two methods [11-18], we have analyzed the economic impact of the two clinical pathways in the management of breast cancer.

A radioactive tracer, according to the Italian Law, may be managed and injected only in a Nuclear Medicine department. These highly specialized structures are not in every hospital available, on the contrary, in Italy, they are available just in the biggest ones. This is the reason why Patients undergo a sometimes long travel to reach the place where the tracer injection will be delivered. Moreover, as it is a potentially dangerous drug both for environment and for the Patient herself, a clinical observation is for a couple of hours necessary, and this requires the use of a hospital bed. Patients, once dismissed, have to travel back home and then, the day after, they have to drive to a second hospital where surgery will take place.

This traffic constitutes not only a cost for Patients and relatives, but also a work overload for centralized structures which carry on other procedures and therapies as well. The travel to the Nuclear Medicine, often by car, is a possible source of an environmental pollution called carbon footprint. Indocyanine green allows to avoid a travel to the Nuclear Medicine and to spare a big amount of transport costs. Moreover, it allows to set time slots free, useful to treat other patients and pathologies, and helps to protect the environment. Under a clinical point of view ICG is a safe tracer, as it has a sensibility and specificity equal to Technetium; if we consider its cost-effectiveness, ICG is also cheaper as Technetium, especially considering peripheric centres or hospitals without Nuclear Medicine. Considering our results, we can suggest the use of Indocyanine green as a detector for breast sentinel lymph nodes for its safety and cost-effectiveness.

### Conflict of Interests Statement

All Authors declare no conflict of interests

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