National equipment of intraoperative gamma detection in the identification of sentinel lymph node in animal model

Equipamento nacional de detecção gama intra-operatória na identificação de linfonodo sentinela

Paula Cristina Fada dos SantosI, Ivan Dunshee de Abranches Oliveira SantosII, Fábio Xerfan NahasIII, Renato Santos de Oliveira FilhoIV, Lydia Masako FerreiraV

I Fellow Master degree, Post-graduate Program on Plastic Surgery, UNIFESP, Sao Paulo, Brazil.
II PhD, Head, Division of Plastic Surgery, Department of Surgery, UNIFESP, Sao Paulo, Brazil.
III PhD, Affiliate Professor, Division of Plastic Surgery, Department of Surgery, UNIFESP, Sao Paulo, Brazil.
IV PhD, Faculty of Medicine, University of Sao Paulo, Brazil.
V PhD, Full Professor, Head, Division of Plastic Surgery, Department of Surgery, Coordinator of the Post-graduate Program on Plastic Surgery, UNIFESP, Sao Paulo, Brazil.

ABSTRACT

Purpose: To investigate a national equipment of intraoperative gamma detection in the identification of sentinel lymph node.

Methods: Thirty young adult male rats were used. After anesthetized, animals were divided into two groups of 15 animals each. Animals from group A received dextran 500 - Tc99 radiopharmaceutical and patent blue V and those from group B received only patent blue V to map the lymphatic drainage. The presence of radiation in the background area, in the area of injection and of the ex vivo sentinel lymph node of group A were measured. After the exeresis, each lymph node in group A and in group B was mixed forming a new random sequence and the radioactive reading of each lymph node was carried out, using both pieces of equipment.

Results: The hottest sentinel lymph node was identified by the national equipment when radiation was measured in the area of lymphatic drainage after the Dextran 500 was injected. Also, the ex vivo sentinel lymph node. The national equipment has also detected radiation in the lymph nodes that had not received radiopharmaceutical, leading to false positive, checked by the application of Mann-Whitney tests and Student’s paired t-tests. The Cronbach alpha has shown high internal consistency of data 0,9416.

Conclusions: The national equipment of intraoperative gamma detection identifies the LS and showed false positives LS and needs improvement.

Key words: Sentinel Lymph Node Biopsy. Equipment. Research Design. Rats.
Introduction

The use of intraoperatory gamma detection has already been established in oncology to identify sentinel lymph nodes in melanoma\textsuperscript{1-4}, in breast cancer\textsuperscript{5-10} and its application for other tumors such as vulva\textsuperscript{11-16}. Also, its use in head and neck\textsuperscript{17} cancer is being studied. Today the sentinel lymph node biopsy procedure is considered to be essential and indispensable. Besides its high sensitivity to detect lymph nodes, the IGD allows for lower dissection, making the procedure less invasive. The SLB has reduced the number of unnecessary radical lymphadenectomies, thus reducing the surgical morbidity\textsuperscript{3,7,12-16}.

The sentinel lymph node (SL) is defined as the first lymph node of the lymph nodal basis to which the drainage of the primary tumor occurs\textsuperscript{17,18}. The SLB in melanoma was established by Morton \textit{et al.}\textsuperscript{19}, at first only using the vital blue dye that allows for the microstaging of solid tumors. These tumors, in the beginning, spread preferably through the lymphatic system. The IGD has already been included in the official staging of melanoma and of breast cancer in accordance with the AJCC/UICC (American Joint Committee on Cancer Staging System)\textsuperscript{20}.

The combination of the lymphatic mapping with the vital blue dye and the intraoperative gamma detection in the SBL has been shown as a more sensitive combination of methods to detect SL\textsuperscript{4,7,8,10,21-23}. The accuracy to find the SL with this association is high, ranging between 98-100\%\textsuperscript{24-30}.

Today, there are several pieces of equipment commercially available to carry out the intraoperative gamma detection such as Neoprobe\textsuperscript{8}, Europrobe\textsuperscript{8}, Navigator\textsuperscript{8}. However, most pieces of equipment are imported and expensive, which a lot of times limits their use to large centers\textsuperscript{31,32}. They basically have a probe with a crystal or small gamma camera in one end, which is connected to a portable counter. In our country, Oliveira Filho \textit{et al.}\textsuperscript{31} have developed a piece of national equipment's national IPEN (patent MU8602566-0) model III, was handled in accordance with the instructions of the unit.

The Office of Diagnostic Imaging of the Samaritan Hospital. The equipment's national IPEN (patent MU8602566-0) model III, was handled in accordance with the protocol of the Radiological Protect Unit. The equipment's national IPEN (patent MU8602566-0) model III, was handled in accordance with the instructions of the unit.

Costa \textit{et al.}\textsuperscript{31} have developed a piece of national equipment (UNIIFESP). For the continuation of the study, it was used equipment under study was according to its reference to each piece of equipment and the radiation reading values in both. Use of the equipment under study was according to its instruction's manual.

After the exeresis, the dyed hottest sentinel lymph node of each animal from group A was identified with numbers (from 1 to 15) by the researcher and placed in separate recipients. The other group of 15 animals (group B) underwent only the lymphatic mapping with vital blue dye and sentinel lymph node exeresis, following all the procedures used in group A, except for the injection of the radiopharmaceutical. After the exeresis of the sentinel lymph node of each animal in group B, they were identified with numbers (from 16 to 30) by the researcher and placed in separate recipients.

The 30 lymph nodes numbered from 1 to 30, were randomly distributed forming a new sequence. Another observer, who didn’t know the random sequence of the lymph nodes, measured the radiation in each lymph node with both pieces of equipment.

After the exeresis of the SL, the animals were subjected to euthanasia with a hyper dose of anesthetic. The animals were disposed according to the protocol of the Radiological Protect Unit.

Statistical analysis

To check discrepancies between the results reached with the conventional equipment and the IPEN equipment, Mann Whitney tests were used. The discrepancies between the pairs of results measured with the conventional piece of equipment were compared to the IPEN piece of equipment were evaluate using the
Student’s paired t-test. The Cronbach Alpha was applied to check the internal consistency of the data. Five percent was used as the level of significance.

Results

The IPEN equipment detected radiation even in lymph nodes which had not received the radiopharmaceutical, leading to a false-positive, as verified by the Mann-Whitney’s test and Student’s paired-t test. This was found when the values of gamma radiation measured with the pieces of intraoperative gamma detection equipment of each ex vivo sentinel lymph node were analyzed (Table 1). The Cronbach Alpha showed a high internal consistency of the data (0.9188). In background area (Table 2), the Cronbach Alpha showed a low internal consistency of data (0.4690).

In the area of the injection, a discrepancy between the pairs of results of both pieces of equipment (p=0.0013) was observed, but Mann-Whitney’s test could not detect differences between the two groups of results (Table 3). The Cronbach Alpha showed high internal consistency of data (0.9416).

Although both devices determined which was the SL, no statistical significant differences were found between the gamma radiation values of the ex vivo sentinel lymph node by the two pieces of intraoperative equipment (Table 4). The Cronbach Alpha showed high internal consistency of data (0.9251).

Discussion

The use of radioguided surgery in the intraoperative location of the sentinel lymph nodes has brought new possibilities in the treatment of tumor metastases. There are criteria that guide the evaluation of radioguided probes in this type of application and define the minimum necessary requirements. The Nema Standards Publication Nu 3-2004: Performance Measurements and Quality Control Guidelines for Non-Imaging Intraoperative Gamma Probes published by the National Electrical Manufacturers Association aims at standardizing performance measurements of radioguided probes for intraoperative use.

The intraoperative gamma detection probe 

The intraoperative gamma detection probe developed by Costa et al. has shown that the physical characteristics have met the suggested proposals in international publications to be used as radioguided probes in the location of sentinel lymph nodes, marked with \(^{99m}\text{Tc}\).

Oliveira-Filho et al. described that the sentinel lymph node is found in around 83% to 100% of the cases, varying according to the location of the region of the sentinel lymph node. In the inguinal cases, 100% of success was reached only

| TABLE 1 – Comparison between the values of gamma radiation reading using the international and the IPEN intraoperative gamma detection equipments of each extirpated sentinel lymph node |
|-----------------|-----------------|-----------------|
|                | International   | IPEN            |
| n               | 30              | 30              |
| Average         | 29.6            | 40.2            |
| Standard Deviation | 38.9          | 26.5            |
| Median          | 8.5             | 26.0            |
| Minimum         | 0               | 13              |
| Maximum         | 116             | 93              |

Mann-Whitney Test U = 293.0 p=0.020

Cronbach’s Alpha = 0.9188

* Statistically significant difference

| TABLE 2 – Comparison between the values of radiation reading in the background of injection by using the International and the IPEN |
|-----------------|----------------|----------------|
|                | International  | IPEN           |
| n               | 15             | 15             |
| Average         | 3.7            | 23.5           |
| Standard Deviation | 1.4          | 8.2            |
| Median          | 4.0            | 27.0           |
| Minimum         | 2              | 11             |
| Maximum         | 6              | 33             |

Mann-Whitney Test U = 0.0 p<0.00001

Cronbach’s Alpha = 0.469

* Statistically significant difference

| TABLE 3 – Comparison between the values of radiation reading in the injection area using the International and the IPEN intraoperative gamma detection equipment |
|-----------------|----------------|----------------|
|                | International  | IPEN           |
| n               | 15             | 15             |
| Average         | 2824.7         | 3901.5         |
| Standard Deviation | 1799.8       | 2583.9         |
| Median          | 3639.0         | 4688.0         |
| Minimum         | 557            | 729            |
| Maximum         | 5176           | 7142           |

Mann-Whitney Test U = 68.0 p=0.067-ns

Cronbach’s Alpha = 0.9416

* Statistically significant difference

| TABLE 4 – Comparison between the values of radiation reading of the ex vivo SLN using the International and the IPEN intraoperative gamma detection equipment |
|-----------------|----------------|----------------|
|                | International  | IPEN           |
| n               | 15             | 15             |
| Average         | 78             | 80             |
| Standard Deviation | 45.9          | 30.4           |
| Median          | 76             | 76.5           |
| Minimum         | 31             | 10             |
| Maximum         | 129            | 161            |

Mann-Whitney Test U = 112.0 p=1.00-ns

Cronbach’s Alpha = 0.9251

* Statistically significant difference
with the vital blue dye, but in other locations the lymph cintillography and the intraoperatory gamma radiation detector are important. The internal consistency of each piece of equipment was studied by means of the Cronbach Alpha analysis. The high internal consistency of data of each extirpated sentinel lymph node was 0.9188 and the low internal consistency of data in the area of the background area was 0.4690 (Table 2).

The IPEN equipment detected radiation even in lymph nodes that had not received the radiopharmaceutical, leading to a false positive, as verified by the application of Mann-Whitney's test and Student’s paired-t test. On the other hand, The IPEN equipment found radiation and the hottest sentinel lymph node by means of sound guidance and also the number scale showed a level above the background values.

Costa et al. reported that because of the high penetrability of gamma rays, radiation can be detected in any part of the patient and not only at the desired area. This situation implies that the detection should not only present high energy resolution, but also the capability to spatially reject undesirable gamma rays which might be reflected over the detector. Therefore false positive readings can be found in normal areas with radioactivity, leading to a diagnostic error.

These results give basis to the possibility to use the national intraoperatory gamma detection equipment in human beings.

Conclusions

1. The national equipment of intraoperatory gamma detection identifies the LS;

2. The national equipment of intraoperatory gamma detection showed false positives LS and needs improvement.

Certainly, this study will serve as the basis to use the national equipment to identify the sentinel lymph node in human beings so that the procedure can become more accessible and less expensive.

References


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Correspondence:
Paula Cristina Fada dos Santos
Division of Plastic Surgery, Department of Surgery
Federal University of Sao Paulo
Rua Napoléon de Barros, 715/4º andar
04024-0022 Sao Paulo – SP Brazil
Phone: (55 11)5576-4065/5576-4118
ppfada@hotmail.com

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