Scientific Research Publishing

Open Journal of Biophysics, 2024, 14, 73-77
https://www.scirp.org/journal/ojbiphy
ISSN Online: 2164-5396
ISSN Print: 2164-5388

Near-Infrared Fluorescence Imaging Contrast Agents for Clinical Research: Limitations and Alternatives

Serigne Moussa Badiane[1*], Elhadji A. L. Bathily[2], Fawrou Seye[3], Louis A. D. Diouf[2]

[1]Department of Health Sciences, Gaston BERGER University, Saint-Louis, Senegal
[2]Department of Health Sciences, Cheikh Anta DIOP University, Dakar, Senegal
[3]Cell Biology and Histology, Health Sciences Department, Gaston BERGER University, Saint-Louis, Senegal
Email: *moussa.badiane@ugb.edu.sn

How to cite this paper: Badiane, S.M., Bathily, E.A.L., Seye, F. and Diouf, L.A.D. (2024) Near-Infrared Fluorescence Imaging Contrast Agents for Clinical Research: Limitations and Alternatives. *Open Journal of Biophysics*, **14**, 73-77.
https://doi.org/10.4236/ojbiphy.2024.141004

Received: December 7, 2023
Accepted: January 27, 2024
Published: January 30, 2024

Abstract

Introduction: Near-infrared fluorescence imaging is a technique that will establish itself in the short term at the international level because it is recognized for its potential to improve the performance of surgical interventions, its moderate investment and operating costs and its portability. Although the technology is now mature, there is currently the problem of the availability of contrast agents to be injected IV. The aim of this methodology article is to propose an alternative solution to the need for contrast agents for clinical research, particularly in oncology. **Methodology:** They consist of coupling a fluorescent marker in the form of an NHS derivative, such as IR DYE manufactured in compliance with GMP, with therapeutic monoclonal antibodies having marketing authorization for molecular imaging. For a given antibody, the marking procedure must be the subject of a validation file on the final preparation filtered on a sterilizing membrane at 0.22 µm. Once the procedure has been validated, it would be unnecessary to repeat the tests before each clinical research examination. A check of the marking by thin-layer chromatography (TLC) and place it in a sample bank at +4˚C for 1 month of each injected formulation would be sufficient for additional tests if necessary. **Conclusion**: Molecular near-infrared fluorescence imaging is experiencing development, the process of which could be accelerated by greater availability of clinical contrast agents. Alternative solutions are therefore necessary to promote clinical research in this area. These methods must be shared to make it easier for researchers.

Keywords

Fluorescence Imaging, Contrast Agents, Clinical Research

1. Introduction

Near-infrared fluorescence imaging is a technique that will establish itself in the short term in clinical practice at the international level because it is recognized for its potential to improve the performance of surgical interventions, its investment and operating costs moderate and its portability. Researchers continue to explore new applications for NIR imaging, whether in the field of neuroimaging, image-guided therapy, or other emerging areas. It is today a strategy aimed at reducing geographic inequalities in the face of cancer. For all these reasons, translational and clinical research work in fluorescence imaging arouses great interest for the development of new diagnostic and therapeutic strategies. It is in this sense that NIR-specific nanoparticles and contrast agents are being developed to target specific biomarkers, thereby improving the sensitivity and specificity of imaging.

However, the limited number of contrast agents authorized for use in humans is a major constraint. Hence the interest in proposing alternatives and strategies to overcome these difficulties.

2. Context

Although the technology is now mature, there is currently the problem of the availability of contrast agents to be injected intravenously. Only Indocyanine Green (ICG) [1] and Methylene Blue [2] currently have marketing authorization in most countries as illustrated in **Figure 1** for the detection of the sentinel lymph node in breast cancer by fluorescence imaging using ICG. These are useful tracers for lymphatic and vascular identification but they do not allow specific molecular imaging which constitutes the main interest in oncology of this modality. However, near-infrared wavelengths allow better penetration through biological tissues, reducing light scattering and providing better depth resolution. Likewise, biological tissues absorb less light in the NIR range, thereby reducing unwanted auto-fluorescence.

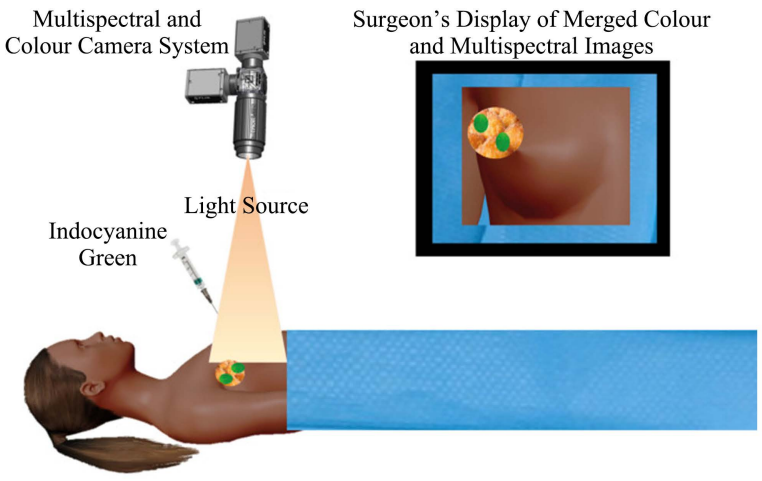

Figure 1. Fluorescence-guided SLNB Using Indocyanine Green. [5]

Currently, numerous multicenter clinical research studies are currently underway with some molecular probes manufactured in accordance with the principles and guidelines to be respected for medicinal products for human use [3] [4].

3. Alternative and Methodological Approach

They consist of coupling a fluorescent marker in the form of an NHS derivative, such as IR DYE 800 CW [6] manufactured in compliance with GMPs, with therapeutic monoclonal antibodies having marketing authorization for molecular imaging [7].

The marking is particularly simple since it involves, on an aliquot of the antibody and under sterile conditions, deprotonating the NH_2 functions of the antibody by adding $NaHCO_3$ QSP pH 8.6 to incubate for 12 hours at +4˚C with NHS fluorochrome in limiting quantities in **Figure 2**.

For a given antibody, the marking procedure must be the subject of a validation file on the final preparation filtered on a sterilizing membrane at 0.22 µm and covering:

- The quality of the marking and quantification of the free fraction of the fluorochrome (CCM or HPLC),
- Preservation of the immuno-reactivity of the fluorescent antibody, by FACS on tumor line cells Human expressing the antigen of interest,
- The absence of oligomerization of the fluorescent antibody (HPLC on a diffusion exclusion column),
- Control (if possible) by *in vivo* fluorescence imaging on mice xenografted subcutaneously with tumor cells of the line selected for the FACS immunoreactivity test,
- Sterility controls (culture) and absence of pyrogens (Limulus test).

Once the procedure has been validated, it would be unnecessary to repeat the tests before each clinical research examination. A check of the marking by TLC and the placing in the sample library at +4˚C for 1 month of each injected formulation would be sufficient for additional tests if necessary.

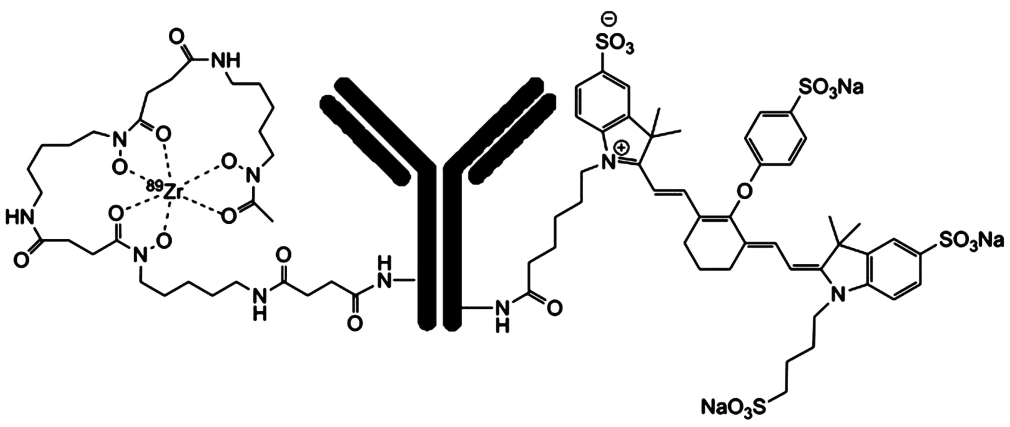

Figure 2. Schematic representation of 89 Zr-mAb-IRDye800 CW. [8]

Note that monoclonal antibodies play a crucial role in tumor targeting imaging, a technique that aims to specifically visualize cancer cells or tumor tissues using contrast agents. They are designed to bind specifically to antigens on the surface of tumor cells. This gives high targeting specificity, allowing precise discrimination between cancer cells and healthy tissues. The use of monoclonal antibodies in molecular imaging allows visualization of specific biomarkers associated with malignancy. This may include antigens specific to certain tumors or proteins overexpressed in cancer cells.

4. Conclusion

Molecular near-infrared fluorescence imaging is experiencing development, the process of which could be accelerated by the process of which could be accelerated by obtaining more clinical contrast agents. Alternative solutions are therefore necessary to promote clinical research in this area. These methods must be shared to make it easier for researchers. Researchers continue to explore new applications for NIR imaging, whether in the field of neuroimaging, image-guided therapy, or other emerging areas.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Azaïs, H., Bats, A.-S. and Koual, M. (2023) New Drug Approval in Surgery: Indocyanine Green for Axillary Sentinel Lymph Node Fluorescence Detection in Breast Cancer. *Bulletin du Cancer*, **110**, 595-596. https://doi.org/10.1016/j.bulcan.2023.03.022

[2] Wang, K., Du, Y., Zhang, Z.Y., *et al.* (2023) Fluorescence Image-Guided Tumour Surgery. *Nature Reviews Bioengineering*, **1**, 161-179. https://doi.org/10.1038/s44222-022-00017-1

[3] Yi, X.M., Wang, F.L., Qin, W.J., *et al.* (2014) Near-Infrared Fluorescent Probes in Cancer Imaging and Therapy: An Emerging Field. *International Journal of Nanomedicine*, **9**, 1347-1365. https://doi.org/10.2147/IJN.S60206

[4] Fushiki, H., Yoshikawa, T., Matsuda, T., *et al.* (2023) Preclinical Development and Validation of ASP5354: A Near-Infrared Fluorescent Agent for Intraoperative Ureter Visualization. *Molecular Imaging and Biology*, **25**, 74-84. https://doi.org/10.1007/s11307-021-01613-0

[5] Kedrzycki, M.S., Leiloglou, M., Ashrafian, H., *et al.* (2021) Meta-Analysis Comparing Fluorescence Imaging with Radioisotope and Blue Dye-Guided Sentinel Node Identification for Breast Cancer Surgery. *Annals of Surgical Oncology*, **28**, 3738-3748. https://doi.org/10.1245/s10434-020-09288-7

[6] Leung, K. (2012) IRDye 800CW-Human Serum Albumin.

[7] Breedveld, F.C. (2000) Therapeutic Monoclonal Antibodies. *The Lancet*, **355**, 735-740. https://doi.org/10.1016/S0140-6736(00)01034-5

[8] Cohen, R., Stammes, M.A., de Roos, I.H.C., *et al.* (2011) Inert Coupling of IR-Dye800CW to Monoclonal Antibodies for Clinical Optical Imaging of Tumor Targets. *EJNMMI Research*, **1**, Article No. 31. https://doi.org/10.1186/2191-219X-1-31