Oral Oncology 57 (2016) 32–39

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Review

Image guided surgery in the management of head and neck cancer

Hassan Iqbal *, Quintin Pan *

Department of Otolaryngology-Head and Neck Surgery, The Ohio State University Wexner Medical Center and Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA

ARTICLE INFO

Article history:
Received 28 December 2015
Received in revised form 11 April 2016
Accepted 12 April 2016
Available online 25 April 2016

Keywords:
Image guided surgery
Near infrared fluorescence
Fluorescence molecular imaging
Sentinel lymph node
Head and neck neoplasm
Squamous cell carcinoma

SUMMARY

Complete resection of head and neck tumors relies on palpation and visual inspection. Achieving a negative margin in remote locations in the head and neck region, especially in close proximity to critical structures, is often difficult to achieve. Positive resection margins in head and neck cancer are at high risk to develop recurrent disease and associated with poor prognosis. Near-infrared fluorescence-guided optical imaging is an emerging technology with the potential to move the surgical field forward and facilitate surgeons to visualize tumors in real-time intra-operatively. In this review, our focus is to discuss the recent advances and the potential application of near infrared (NIR) fluorescent-guided surgery in the management of head and neck cancer.

© 2016 Elsevier Ltd. All rights reserved.

Introduction

The worldwide incidence of head and neck neoplasm is 900,000 new cases with more than 55,000 newly diagnosed cases reported in the United States each year [1–3]. Surgery, pharmacotherapy, and radiotherapy are regarded as the standard of care for the management of head and neck squamous cell carcinoma. The aim of surgical resection of the tumor is to completely remove the tumor, preserve the normal tissue, and consequently achieve a clear tumor-free resection margin. Surgeons have to rely on visual inspection, palpation, and experience but majority of the time, it is very difficult to remove the tumors in remote anatomical locations or places in close vicinity to critical structures even in expert hands. Achieving adequate clear margins are critically important and have significant prognostic impact [4]. The head and neck region is unique from the rest of the body in respect to the location of vital structures, such as cranial nerves and major vessels supplying the brain, in close vicinity to each other. Getting a close or involved margin influences the prognosis whereas resecting the tumor with wider margins may impact normal function and increase morbidity. The incidence of close or positive margins has remained largely unchanged over the years and can be as high as 40% [5,6]. To determine a positive or a close margin either the surgeons have to wait for the histopathology report several days later or perform an intraoperative frozen section analysis. To analyze the wound bed for frozen section, the tissue specimens are taken randomly and surgeons have to reply on only visual inspection. Although great progress has been made in visualizing the tumor extent and its spread with the use of CT, MRI and PET scans, nevertheless there is a lack of intra-operative imaging tools that can help the surgeon to visualize and guide the excision of the tumor with better margin control in real time.

A relatively new technology that is evolving is the invisible near-infrared (NIR) fluorescent light. In the intraoperative setting, fluorescence molecular imaging (FMI) is of great utility and can be used to guide the surgeon to easily distinguish between normal and malignant tissue. Recent work has shown that FMI can facilitate the surgeons to excise the tumors at a sub-millimeter size [7,8]. For its intraoperative applicability the most important aspects of the FMI are the imaging contrast and surgical navigation. The aim of this review is to report the various fluorescent dyes and optical systems used in image guided surgery. In the latter half of this review, the evolving role of fluorescent imaging and image guided surgery in the management of head and neck cancer are discussed.

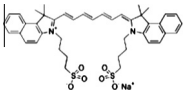
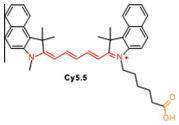
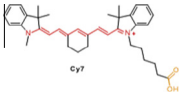
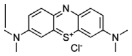
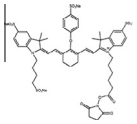
Fluorescent dyes and probes

A fluorescent dye should possess certain properties to build an optimal image for image-guided surgery. A summary of properties of various different fluorescent dyes is shown in Table 1. Ideal

* Address: The Ohio State University Wexner Medical Center, Department of Otolaryngology-Head and Neck Surgery, 420 West 12th Avenue, Columbus, OH 43210, USA.
E-mail addresses: iqbal.56@osu.edu (H. Iqbal), Quintin.Pan@osumc.edu (Q. Pan).

http://dx.doi.org/10.1016/j.oraloncology.2016.04.007
1368-8375/© 2016 Elsevier Ltd. All rights reserved.

Table 1
Structure and characteristics of NIR fluorescent dyes.

	NIR fluorescent dyes					
	Indocyanine green	Cy5.5	Cy7	Methylene blue	Irdye 800 CW	Quantum Dots (nanoparticles)
Structure						Depends on structural characteristics
Molecular weight (Da)	320	1069	720	320	45–200	Not applicable
Excitation wavelength (nm)	779	675	794	550	775	Broad absorption spectrum
Emission wavelength (nm)	806	695	775		796	808
Net charge	−1	−4	−3	+1		Depends on structural characteristics
High quantum yield	Mild	Moderate	Moderate		Moderate	High
Aqueous solubility	Soluble	Soluble	Soluble		Soluble	Soluble
Hydrodynamic diameter (nm)	<1	<1	<1	<1		Depends on structural characteristics
Clearance	Hepatic	Hepatic	Hepatic	Hepatic		Depends on structural characteristics
Toxicity	Low	Low	Low	Low	Low	
Low photo-bleaching	Moderate	Moderate	Moderate		Moderate	Strong
Extinction Coefficient (M^{-1} cm^{-1})	121,000	166,000	196,000	71,200	237,000	Depends on structural characteristics

properties of fluorescent probe include high affinity for its target, fast clearance from the blood, better bio-distribution, and tumor specificity. Also, a fluorescent dye should have sufficient solubility to reach the intravascular compartment and lymphatic channels. Another key property for fluorescent dye is a high quantum yield; more photons emitted then absorbed. Dye that possess quantum yield of less than 0.1 will have inadequate emission. The ideal emission wavelength for fluorescent dyes for image-guided surgery is between 700 and 900 nm (near NIR region) [9]. Above 900 nm, water absorbs this wavelength and thus significantly reducing the light transmission. Wavelengths of less than 100 nm are extremely low to be detected beyond a few micrometers of tissue penetration. Lastly, a fluorescent dye should possess a high signal-to-background ratio. Signal-to-background ratio is reduced when the dye binds to nonspecific cellular structures like cell membranes or proteins.

Various different fluorescent dyes have been tested such as ICG, Cy5.5, Cy7, Irdye800 CW, and ProSense 750. ICG has been the most extensively used in the humans [10] and in various different studies since 1970, showing its diverse clinical applicability [11–14]. ICG has a short lifetime in the blood (2–4 min plasma half-life) and slow plasma clearance rate once bound to the plasma proteins [15]. Earlier, ICG was used to assess cardiac and liver functions and lately, its applications have been diversified to visualize bile ducts, vascular networks, and demarcation of liver segments [16–19]. Although various NIR fluorescent contrast agents have been developed and tested in preclinical studies only ICG is approved by the FDA for fluorescence imaging [20]. The use of ICG has been extensively studied in hepatocellular carcinoma (HCC) and metastatic colorectal carcinoma (MCC). ICG has a unique ability to accumulate in the HCC tumors and in MCC it forms a rim around the liver metastatic deposits [21]. Intraoperative ultrasound is often used in localizing the hepatic lesions but its main disadvantage is the inability to detect small and superficial lesions. NIR fluorescence has gained popularity since it is more sensitive in identifying superficial and small hepatic tumors [21]. Other studies conducted have confirmed the sensitivity of fluorescent imaging after ICG injection in identifying liver lesions, however, a caveat is that all the detectable liver metastatic lesions were close to the surface (less than 8 mm) [22,23]. Wapnir et al. conducted a study utilizing ICG and an infrared camera system (SPY Elite™) to intraoperatively evaluate the skin perfusion in nipple sparing mastectomies. They concluded that visualization of tissue perfusion can reduce ischemic complications and moreover, this approach can be used as a navigation tool to design mastectomy incisions [57]. Perfusion imaging in breast reconstruction has shown to be cost effective and now, has been widely adopted since this is a reimbursable procedure.

Research has been conducted in conjugating the NIR fluorescent agents to monoclonal antibodies targeted against epidermal growth factor receptor (EGFR), human epidermal growth factor receptor-2 (HER2), vascular endothelial growth factor (VEGF) receptor, thus facilitating the development of new generation of molecularly-targeted NIR fluorescent probes [24–26]. Currently an ongoing trial is recruiting breast cancer patients for the imaging using bevacizumab, an anti-VEGF antibody, conjugated to IRDye 800 CW [27]. The purpose of this trial is to determine the safety and uptake of bevacizumab-IDRye800 CW in breast cancer tissue. Currently, there are two NIR fluorophores that are being investigated in the clinical setting: IRDye 800 CW and ZW800-1 [28]. Both of these fluorophores can be conjugated to target ligands to make a molecularly targeted NIR probe to use in an intraoperative setting.

The adaptation of nanotechnology in the fluorescence imaging field has opened up potential new avenues in the field of medical imaging and fluorescent guided surgery. Nanotechnology has various benefits over low molecular weight fluorescent dyes such as size, which helps in better bio-distribution, and brightness. An interesting finding of the nanoparticles is that, they show enhanced permeability and retention (EPR) resulting in enhanced tumor accumulating compared to low molecular weight fluorophores [20]. Another advantage of nanostructures is their high image contrast and improved optical properties of the tracer. Nano-tracers can be constructed either with the use of intrinsically fluorescent semi conducting nanocrystals (quantum dots) or binding of low molecular weight fluorophores to silica or organic nano-templates. A wide range of nano-probes have been constructed such as quantum dots, dye-loaded inorganic nanocarriers, dye loaded organic carriers, polymer based nanoparticles, lipid based nanoparticles and it is out of scope of this review article to comprehensively review all of them. Although quantum dots are

Download English Version:

https://daneshyari.com/en/article/3163738

Download Persian Version:

https://daneshyari.com/article/3163738

Daneshyari.com