Disponible en ligne sur
ScienceDirect
www.sciencedirect.com
Elsevier Masson France
EM|consulte
www.em-consulte.com
IRBM
IRBM 37 (2016) 131–143

General Review

On Image Segmentation Methods Applied to Glioblastoma: State of Art and New Trends

C. Dupont [a,*,1], N. Betrouni [a,2], N. Reyns [a,b,3], M. Vermandel [a,b,2]

[a] *Univ. Lille, Inserm, CHU Lille, U1189 - ONCO-THAI - Image Assisted Laser Therapy for Oncology, F-59000 Lille, France*
[b] *CHU Lille, Neurosurgery Department, F-59000 Lille, France*

Received 29 September 2015; received in revised form 16 December 2015; accepted 16 December 2015

Available online 8 January 2016

Abstract

Because of high heterogeneity and invasiveness, treatment of GlioBlastoma Multiform (GBM) still remains a complex challenge. Several recent advanced therapies have improved precision of treatment deliverance. Multimodality imaging plays an increasingly important role in this process and images segmentation has become an essential part of the pipeline of standard treatment planning system. With the sophistication of multimodality information, the development of reliable and robust segmentation algorithms to overcome manual segmentation and optimize targeted treatment is highly expected.

In this paper, we first introduce targeted therapies applied in the GBM clinical care, from routine or research. Different segmentation methods from state of the art are highlighted to achieve GBM delineation. New trends in GBM segmentation such as machine learning and multimodal features are discussed. These additional frameworks may achieve segmentation with refining capacities, active tumour probability mapping and, even, tumour relapse prediction capacities.

Keywords: Segmentation; Neuro-oncology; Radiation oncology; High-grade glioma treatment; Targeted therapies

1. Introduction

Central nervous system (CNS) cancer is the 10th leading cause of death by cancer in the population over 20 years. Gliomas represent about 3% of premature cancer death (aged less than 65) and is the 3rd cause of death by cancer for young adults (aged between 15 and 34) [1]. Among them, Glioblastoma Multiform (GBM) is the most common tumour with a very poor prognosis (median survival below 18 months). About 12 000 in the USA [2] are annually diagnosed and its incidence is estimated at 5 to 7 new cases each year for 100 000 inhabitants [3]. Nowadays, the main goal of the therapy is to improve lifespan while maintaining a decent quality of life for patient bearing GBM [3].

In this context and on behalf the European Organization for Research and Treatment of Cancer-National Cancer Institute of Canada (EORTC-NCIC), Stupp et al. [4] proposed a specific treatment protocol for high grade glioma. This protocol combined 3 main therapies: surgery, radiotherapy and chemotherapy. Nowadays, this combination still remains the standard protocol in the management of GBM.

The quality of surgery is a documented prognostic factor of survival [5]. However, even in adequate removal, the invasive nature and rapid proliferation of GBM do not allow its control by conventional treatment protocols. Patients whose tumour location does not allow for tumour resection have then a limited survival.

Thus, the main issue for the treatment of GBM relies on its very heterogeneous tumour tissue properties (see Fig. 1). GBM is made of a macroscopic component, the tumour bulk, and

* Corresponding author.
E-mail address: clement.dupont@inserm.fr (C. Dupont).
[1] PhD student.
[2] PhD.
[3] MD, PhD.

http://dx.doi.org/10.1016/j.irbm.2015.12.004
1959-0318/

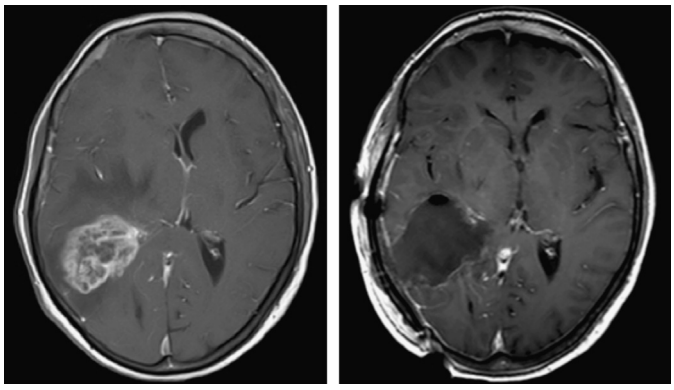

Fig. 1. Pre-operative MRI showing a high-grade glioma located in associative areas and ventricular crossroad. On the right, early post-operative control (<72 h) with no more contrast enhancing tumour.

a component infiltrating the surrounding tissue. Furthermore, oedema surrounding the tumour may also be partially infiltrated with tumour cells. The differentiation between oedema, healthy tissue and tumours cells is a major issue when considering local therapy based on target definition such as radiation oncology [4], laser therapies [6], High Intensity Focused Ultrasound (HIFU) [7]. As, no segmentation approach can fit all brain tumour type, GBM segmentation results in specific strategy to manage its heterogeneous properties.

We propose here a review of methods developed to address the issue of GBM segmentation. First, we introduce the therapies, based on target delineation, in use to tackle GBM. Then, we present different methods of segmentation from the literature. Finally, we highlight the new trends in GBM segmentation and discuss the rational of using approaches resulting in binary segmentation while addressing infiltrating tumour.

2. Therapies of high-grade gliomas

2.1. Standard protocol

Depending on the GBM location, surgery is firstly achieved. It aims to achieve maximal cytoreduction without affecting the functional prognosis of patients because of their pejorative prognosis (see Fig. 1). After the resection of the tumour bulk, Fluorescence-Guided Resection (FGR) [8–10] can be used to optimize the cytoreduction. FGR relies on the administration of a photosensitizer (or its precursor). FGR is mainly performed using 5-ALA which is the precursor of Protoporphyrin IX (PpIX; use in clinical practice of 5-ALA is authorized since 2007 in Europe, commercial name: Gliolan – Medac, Germany) [11]. PpIX is a photoactive compound that absorbs blue light (404 nm). PpIX is mainly fixed in the tumour cells. Indeed, Photodynamic detection offers 89% sensitivity and 96% specificity [12]. After excitation of the PpIX by a filtered violet-blue light source [13,14], remainder of the tumour shines bright red through the blue surgical field.

Several studies reported its efficacy to achieve complete resection: about 65% of tumour tissue removed [15]. Nevertheless, temporary impairment of neurological function could occur more frequently. Those effects must be compared to the benefits and the impact on the lifespan. It was observed that the degree of surgical resection correlates approximately with the survival probability. Indeed, the progression-free clinical survival increased of about 6 months (6.73 months to 12.88 months) and clinical survival increased of about 8 months (12.3 months to 20.9 months) [16].

In addition to surgery, radiotherapy is delivered [17]. Tumour delineation is required to plan the treatment. First, Gross Tumour Volume (GTV) is easily delineated from T1, T1Gd and T2 weighted. Then, Clinical Target Volume (CTV) is deduced from the GTV. Ballistic optimization is highly sensitive to this CTV but its delineation remains very complex because of the infiltrating component of the Glioma.

Chemotherapy may be also delivered, in addition to the radiotherapy. Most of studies revealed that these adjuvant treatments could not bring solutions for the recovery of a patient. However, chemical application on residual tumour cells after resection surgery can produce an effect on lifespan [18].

2.2. Recent advanced therapies

Recently, High-Intensity Focused Ultrasound (HIFU) has shown interest and significance for the management of high-grade gliomas. HIFU is a targeted treatment based on high-intensity ultrasound [19,20]. This technology consists of focusing high-energy ultrasounds in order to create thermal and mechanical effects on the targeted tissues. It can be delivered extracorporealy, intracavitarly and interstitially. The resulting heat and pressure increase lead to a coagulation necrosis [21]. HIFU have been trained on different pathologies and tissues: glaucoma, pancreas, prostate, liver, thrombolysis, venous insufficiency and brain tumour. A recent study demonstrated its benefit on antitumor effect paired with chemotherapy in the GBM case [7,22].

Since 2002, a new modality has brought the possibility to treat non-resectable GBM using interstitial Photo-Dynamic Therapies (PDT) [23]. PDT is a selective therapy that consists in exposing photosensitized tumour cells to a specific wavelength light. Such exposition aims to generate a cytotoxic effect. Recent developments offer new possibilities for the management of high-grade gliomas [24–26].

In a general manner, PDT can be delivered extracorporealy, intracavitarly or interstitially [27]. This therapy has been trained on other localizations like prostate cancer [28,29], lung cancer [30] or dermatology [31,32]. PDT relies on three main parameters:

- **Photosensitizer** (PS): previously administered to the patient, leads to a photosensitizer, preferentially fixed in the tumour site. Several studies [23,33–36] reported the use of a precursor, 5-AminoLevulinic Acid (5-ALA). 5-ALA induced a specific uptake of the PS: the Protoporphyrin IX (PpIX). Significant difference of PS concentration between healthy and tumour tissues led to a selective treatment.
- **Light**: illumination to an appropriate wavelength (corresponding to the red visible light, between 620 to 690 nm) is the cornerstone that brings the required energy for the