Segmentation of Nodular Medulloblastoma Using Random Walker and Hierarchical Normalized Cuts

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Abstract—**Medulloblastoma (MB) is the most common brain tumor in children. Recent studies have demonstrated a relationship between specific signaling pathway abnormalities, a tendency to more favorable outcomes, and a histopathological feature: nodular growth patterns. In this work we present a new segmentation scheme which requires minimal user interaction to segment nodules on MB histopathological sections. Our segmentation scheme consists of two steps: (1) color reduction using Hierarchical Normalized Cuts (HNCut), (2) Random Walker (RW) segmentation within the reduced HNCut color space. Across a cohort of 18 nodular MB images, our integrated HNCut and RW scheme yielded nodule segmentations with a Dice coefficient of $83.55 \pm 12.4\%$ and Predictive Positive Value (PPV) of $93.71 \pm 9.0\%$.**

I. INTRODUCTION

Medulloblastoma is a malignant (World Health Organization (WHO) grade IV) embryonal central nervous system (CNS) tumor comprised of primitive neuroectodermal cells involving the cerebellum. MB typically presents between 3-10 years of age and accounts for nearly 25% of all pediatric brain tumors. Currently, histopathological classification of MB includes four subtypes, two of which (desmoplastic nodular and MB with extensive nodularity) are associated with a nodular growth pattern. Desmoplastic nodular MB have been associated with more favorable prognoses [1]. Genomic analysis of MB have established evidence for molecular subtypes of MB based on patterns of signaling pathway activation including Wnt, Shh and others [1] [2]. Based on these studies, a relationship between nodular desmoplastic type MB and Shh signaling pathway abnormalities has been established [3]. The ability to automate the recognition of nodular histopathological features in MB is a first step in establishing computerized image analysis tools to further aid in the development of revised MB classification that incorporates molecular and signaling pathway information to improve current risk based stratification.

Nodules within MB are areas of significantly varied nuclear density in a circular or elliptical shape characterized by a lighter color due to abundant neuropil. Traditional texture based classification schemes may be ill posed to deal with the textural heterogeneity within the nodule and background. Additionally, the irregularity of nodule shapes and diffuse boundaries might limit the ability of traditional shape based active contour schemes to detect the nodular edge without bleeding into the background. The Random Walker (RW) [4] segmentation method is ideally suited for segmenting weak boundaries and creating a continuous edge. However the RW algorithm is typically unable to deal with very high resolution color images (such as digitized Hematoxylin and Eosin (H&E) stained images) on account of computational constraints. The HNCut [5] is a color based segmentation scheme that integrates the mean shift clustering scheme with normalized cuts and allows for rapid and accurate pixel level object selection. By leveraging the strength and efficiency of HNCut, we are able to obtain an initial object (nodule) segmentation which is then provided to the RW algorithm thereby enabling automated and accurate boundary based segmentation of the nodule.

II. METHODS

A. Hierarchical Normalized (HNCut) for Color Based Segmentation

HNCut [5] integrates the Mean Shift (MS) and Normalized Cuts (Ncuts) techniques for pixel-level classification. Briefly it comprises the following main steps.

1) The user defines a color swatch, obtained as a set of representative pixels from the foreground object.
2) MS then leverages the color swatch to identify similar colors in the rest of the image.
3) Ncut calculates an affinity matrix from the MS color space. It then produces a cut with the objective of removing unwanted colors (not part of the foreground).
4) At this point, the HNCut yields a pixel based segmentation of the object of interest (in this case the nodule).
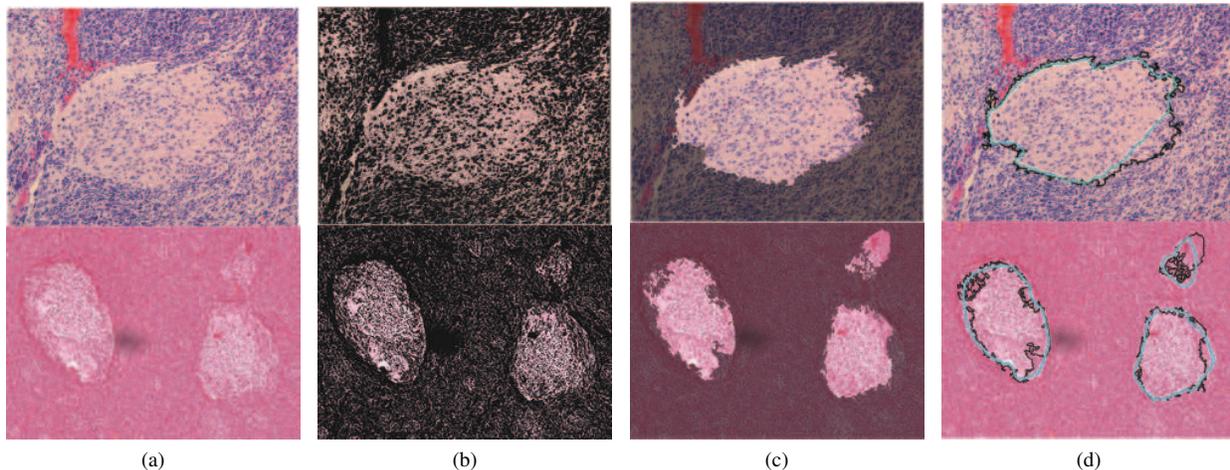
Fig. 1: A MB nodule as seen on (a) the original H&E stained histology (b) color reduced H & E stained histology by HNCut (c) Likelihood map of foreground object (nodule) obtained via RW, and (d) final nodule boundary determined via HNCut and RW (ground truth outline in blue).

B. Random Walker Segmentation

RW [4] is based on the principle that given an infinite number of random paths taken from a certain pixel, a probability can be calculated determining the likelihood of reaching a user defined foreground or background seed. Rather than calculating every possible path in the image, the following algorithm is used:

1) Seed locations are automatically chosen from within the HNCut segmented foreground and background objects.
2) The edges of the nodule are detected across which a random walker cannot pass.
3) A partial differential equation - the Dirichlet equation, is solved with the detected edges as the boundary - simulating the 'random walk' and calculating the probability of each pixel reaching a foreground or background seed.
4) The probabilities are mapped to the same location as the pixels, their grayscale values representing the probabilities.
5) The probability map is then thresholded in an iterative manner to achieve a final, hard segmentation, containing at least 1 foreground seed point, while excluding at least 1 background seed point.

III. EXPERIMENTAL DESIGN AND RESULTS

Histopathological samples stained with H&E from 82 MB cases were obtained from the consultation files of St. Jude Childrens Research Hospital. Representative slides were digitized by whole slide scanning using an Aperio ScanScope slide scanner at 200X magnification. Regions of tumor were then manually extracted which demonstrated MB free of necrosis, hemorrhage or technical artifacts. These areas were subjected to neuropathological review and annotated for the presence of nodular features. This resulted in a set of 18 nodules that were manually segmented to obtain a ground truth mask. They were also segmented using our methodology. Given an image, we compare our segmentation results to the ground truth via (a) Dice Coefficient, (b) Positive Predictive Value (PPV), and (c) Mean Absolute Distance (MAD) between the HNCut + RW segmentation and the ground truth. Table I the Dice, PPV, and MAD values for segmentation over 18 studies.

Evaluation Measure	Quantitative Results
Dice's Coefficient	$83.55 \pm 12.4\%$
PPV	$93.71 \pm 9.0\%$
MAD	6.04 ± 5.50

TABLE I: Quantitative results for 18 nodules on MB for the area based measures, Dice's Coefficient and PPV, and the edge based measure MAD.

IV. CONCLUDING REMARKS

In this paper, we presented a novel approach to segmenting nodules on MB H&E histologic sections. Our methodology consisted of a synergistic combination of HNCut and RW to yield an accurate segmentation of individual nodules. Our approach demonstrated a high level of accuracy with minimal user interaction. The segmentation of MB nodules will allow us to develop more refined tools for automated MB histopathological classification based on features of prognostic and molecular significance.

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