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Correlation Morphometric Feature Analysis in Radiation Oncology

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Abstract

The information related to the shape and size of a tumour can be exploited from the morphometric feature analysis of medical images. The ability of extracting such features from a wide range of imaging modalities enables various clinical applications in radiation oncology. The morphometric features such as volume, surface area, and Surface to Volume Ratio (SVR), sphericity, asphercity, Spherical Disproportion (SD), compactness one and two were useful in detecting and distinguishing benign and malignant lesions, classifying histological subtypes of carcinomas, predicting prognosis and assessing response after therapy. The morphometric features have emerged as promising biomarkers with discriminative and predictive capabilities and their appropriate usage will allow for the development of clinically implementable radiomics models in radiation oncology.

Keywords: Shape; Morphology; Morphometry; Radiomics; Cancer; Tumour

Introduction

Cancer which is a global issue associated with high incidence and high mortality needs effective measures to reduce morbidity and mortality [1]. Yet, the challenge remains in the accurate detection, characterization, treatment and monitoring of cancer makes it difficult to achieve this. However, the radiomics, high-throughput extraction and analysis of large amounts of image features from radiological images have emerged as a promising method that allows for the accurate diagnosis as well proper management strategies [2]. The radiomics features captured from morphometric analysis are important to understand the geometric aspects of a particular tumor Region of Interest (ROI). The appearance of cancer or malignant cells differs from the normal cells due to the abnormality in their size, shape and other features and the increasing abnormalities in morphometry suggest the likelihood of increasing invasiveness [3-5]. Therefore, the morphometric assessment plays a crucial role in cancer detection and management. However, identifying the usefulness, robustness and challenging areas with respect to morphometric features is essential to employ such features in the clinical practice. Therefore, the following review is aimed at providing an overview of the morphometric features with significant findings and challenges encountered in utilization of morphometric features.

Literature Review

Outcomes of morphometric feature analysis

The significant findings related to the individual morphometric features (i.e., volume, surface area, SV, sphericity, asphercity, SD, compactness, maximum 3D diameter, flatness, axis lengths, solidity/volume density based on convex hull, area density based on minimum volume enclosing ellipsoid and Moran's I) are described herein.

Tumor volume is the most commonly evaluated morphometric feature since it is considered to be an important predictor in determining the clinical outcomes [6,7]. The volume was among the optimal parameters for differentiating Breast Carcinoma (BC) and breast lymphoma [8]. Nevertheless, it was not a top contributing feature for classifying histological subtypes of NSCLC [9]. Aerts revealed that the volume had a good prognostic performance for patients with NSCLC and Head and Neck Carcinoma (HNC) but combining the radiomics signature with volume had even better prognostic performance than the use of volume alone [10]. According to Carvalho volume of the Lymph Nodes (LNs) was an independent prognostic factor for NSCLC but not the volume of primary tumour [11]. However, volume was not a predictive feature of pathologic Complete Response (pCR) for NSCLC after neoadjuvant Chemo Radiotherapy (nCRT) [12]. Ulrich also revealed that a favorable prognosis was associated with small tumour volume of patients with Head and Neck Squamous Cell Carcinoma (HNSCC) after chemo radiotherapy (CRT) [13]. According to Yang volume failed to predict pCR for esophageal Squamous Cell Carcinoma (OSCC) after nCRT [14]. In addition, Gabryś showed volume as a useful predictor of long-term Xerostomia in HNC patients treated with radiotherapy while normal tissue complication models based on mean radiation dose failed to predict Xerostomia [15].

Surface area exhibited the highest difference between Grade II and Grade III gliomas in terms of mean rank values [16]. Further, the surface area obtained from margin ROI ranked 3rd among the highest ranking five features for distinguishing recurrent and non-recurrent patients with Prostate Carcinoma (PC) after radiotherapy [17]. As shown by Chad dad it was among five radiomics features that moderately correlated with survival time of large cell carcinoma. Moreover, it was significant in all four groups (i.e., large cell carcinoma, primary tumor size (T2), none LN metastasis (N0), and

TNM stage I) associated with NSCLC survival [18]. Fang selected surface area to construct the radiomics signature which showed the ability for predicting treatment response in patients with locally advanced cervical carcinoma prior to concurrent CRT [19].

Yang suggested that the SVR may provide more information about pCR than tumour volume. Moreover, they revealed that a lower SVR to be indicative of a more compact shape [14]. In addition, lower SVR was shown to be an independent factor differentiating Invasive Adenocarcinomas (IAs) from Minimally Invasive Adenocarcinomas (MIAs) and Adenocarcinomas *In Situ* (AISs) that appear as pure ground-glass nodules (pGGNs) [20]. As shown by Park it was chosen to build the radiomics score that showed significant association with Disease-Free Survival (DFS) in patients with invasive BC. Moreover, they stated that the degree of irregularity of the tumour boundary was quantified by SVR and thus the irregular tumour boundary was likely to be associated with poor survival [21]. In addition, SVR was a dominant feature in predicting LN metastasis in patients with PC after prostate-specific membrane antigen radio-guided surgery [22].

Sphericity was the most important feature across multiple models for discriminating Glioblastoma (GBM) and Brain Metastasis (BM) [23,24]. Further, it was revealed that the sphericity value of GBM is lower than that of BM [24]. Also, it was beneficial in discriminating PC labeled with different Gleason scores [25]. This feature exhibited its usefulness as an independent parameter in distinguishing IAs and MIAs as well [26]. Likewise, radiomics signature constructed by Jiang uniting sphericity with other non-morphometric features showed good discriminative performance in differentiating IAs from MIA in pGGNs with pleural contact [27]. Sphericity was selected to build the radiomics signature which demonstrated significant differentiation between seminomas and non-seminomas according to Zhang [28].

Coroller identified a rounder tumour which was quantified by sphericity as a feature predicting Gross Residual Disease (GRD) and directly proportional to the probability of GRD in patients with NSCLC after nCRT and before surgical resection [12]. Song suggested that the sphericity may reflect histological peripheral distribution of micro papillary patterns within lung adenocarcinomas [29]. Du identified sphericity as the most important risk factor for predicting disease progression in patients with nasopharyngeal carcinoma. They showed that the risk of 3-year disease progression after radiotherapy is increased with decreasing sphericity [30]. Also, it was one of the two most significant predictors of lymphovascular invasion in OSCC [31]. Morin concluded that sphericity had the potential to predict tumour grade, local failure and Overall Survival (OS) in meningioma patients. Low sphericity was linked to increased local failure and worse OS according to them [32].

Asphercity provided better prognostic values for progression free survival and OS in NSCLS patients compared to standardized uptake value, metabolic tumour volume, total lesion glycolysis and solidity [33]. Also, it was associated with poor survival despite palliative systemic treatment in patients with metastatic colorectal carcinoma [34]. Furthermore, asphercity showed the potential to be an independent predictor of prognosis in patients with invasive ductal BC [35].

High SD was significantly associated with high grade meningiomas which exhibited non-spherical shape compared to low grade meningiomas [36]. Chu revealed that the pancreas in pancreatic ductal carcinoma indicated less SD than normal pancreas [37]. SD of the primary tumour site was associated with pCR and GRD in NSCLC patients. Moreover, this feature reflected that the rounder-shaped tumours were less likely to respond well to nCRT [38]. Bogowicz showed that larger SD linked to worse prognosis in patients with HNC. Furthermore, this larger SD indicated larger LN spread and suggested that the SD should be interpreted as a spread of disease than as complexity of LN shape [39]. Ulrich also showed that a favorable prognosis was associated with lower SD in patients with HNC [13]. Moreover, this feature ranked as the feature with the highest importance for predicting OS as well as DFS in patients with GBM [40].

Discussion

Compactness 1 was a significant predictor of pCR in patients with Locally Advanced Rectal Carcinomas (LARC) and poor tumour compactness demonstrated close association with lymph vascular space invasion [41,42]. Also, this was a potential predictive feature for assessing the risk in OS of patients with HNC [43]. In addition, this feature was selected to construct the radiomics signature which exhibited significant prognostic power for patients with Oropharyngeal squamous cell carcinoma [44]. Fave revealed that the prognostic potential of the NSCLC patients was improved by selecting Compactness 2 as a pretreatment feature for OS time and time to distance metastasis models. Furthermore, their study reflected that the larger compactness 2 was associated with a higher predicted risk of experiencing the outcome [45]. Compactness 1 and compactness 2 were useful features to differentiate heart from other normal tissues and tumour volumes in patients with Hodgkin disease and Erwin sarcoma [46].

Aerts identified compactness along with four non-morphometric features to achieve significant prognostic performance in lung and HNC patients but it was not among the most dominant features [10]. However, it was among the top five discriminative features between tumour progression and pseudo progression in patents with GBM [47]. In addition, compactness was selected as a top contributing feature from morphometric features for the classification of NSCLC subtypes [9]. Besides, compactness was associated with OS of gastro-esophageal junction adenocarcinoma treated with nCRT and high compactness was suggestive of low risk while low compactness was suggestive of high risk [48]. Discrete compactness demonstrated higher predictive performance in discriminating encapsulated Thymoma from invasive Thymoma according to Lee [49] but Yamazaki showed that it did not differentiate high risk and low risk Thymoma [50]. Nevertheless, it was identified as a useful parameter for differentiating subtypes of gliomas [51].

Larger maximum 3D diameter was an independent differentiator of lung adenocarcinoma [20]. In meningiomas, it was higher in brain invasion group compared to non-invasion group [52]. Yet, it was not a statistically significant feature for distinguishing histological subtypes of renal carcinomas [53]. As shown by Zhuang maximum 3D diameter was a contributing feature of CT-based radiomics score that differentiated pCR and non-pCR patients with LARC after neoadjuvant treatment compared to clinical variables [54].

Flatness was a contributing feature of the biomarker exhibiting strong and significant performance for discrimination of benign and malignant lung lesions [55]. Similarly, Palumbo found flatness to be significantly differentiating lung nodules and higher values were indicative of malignancy. However, this was applicable for PET-based features whereas CT-based features did not exhibit such significant differentiation [56]. Besides, a favorable discrimination was exhibited between lymphosvascular space invasion and non-lymphovascular space invasion in cervical carcinoma by using the radiomics nomogram in which flatness was the selected morphometric feature [57]. It was identified as a potential biomarker for predicting tumour response after radiotherapy in NSCLC patients as well [58].

The major axis length was identified as an independent prognostic factor for patients with nasopharyngeal carcinoma and its prediction of OS was better than N stage according to Zhai [59]. Except for another non-morphometric feature least axis length was recognized as the most important independent prognostic radiomics feature for nodal control in HNSCC. Furthermore, a larger least axis length of LN was likely to indicate a round-shaped LN rather than an oval-shaped LN with similar volume [60]. Also, it was among the two most significant radiomics features to discriminate patients achieved pCR and non-pCR in locally advanced rectal adenocarcinoma after nCRT [61].

Solidity was a useful feature for the classification of endometrial carcinoma patients with and without LN metastasis [62]. Also, it was a useful predictor for OS of patients with stage III NSCLC by Fried. They presented that the lower solidity was an indication for more dispersion of the tumour [63]. Higher area density based on the minimum volume enclosing ellipsoid was found to be associated with worse OS in patients with Renal Cell Carcinoma (RCC) [64]. Moran's I was an independent prognostic factor for predicting progression free survival and OS in patients with invasive squamous cell carcinoma of vulva [65].

Promises and challenges

The morphometric features were insensitive to normalization as well as to pixel space resampling or interpolation [66,67]. Also, they were less affected by the noise which is favorable for their utilization in radiation oncology [68]. Apart from the usefulness of morphometric features to perform a given task such as discriminating benign and malignant lesions or classifying histological subtypes or predicting prognosis or assessing response to therapy, the robustness and repeatability of these features are important for achieving the optimum benefit in clinical applications. Even though morphometric features had exhibited highest repeatability and robustness [67,69] there are factors affecting their repeatability and robustness. For example, the image sequence or image contrast may impact the robustness and repeatability of a morphometric feature for a particular study [66,70]. In addition to the type of image [71,72], image acquisition parameters [73] and software platform [74] could also affect the reliability of these features. Moreover, the robustness of extracted morphometric features may vary depending on the method of segmentation [75,76]. Lack of standardization and harmonization methods is also a problem in obtaining reliable results [77]. Therefore, it is necessary to take the above factors into consideration when incorporating morphometric features into a radiomics model which would be clinically implementable and acceptable.

Conclusion

The morphometric features have emerged as promising biomarkers with discriminative and predictive capabilities and their exploitation with careful consideration would enhance the clinical benefit in radiation oncology. It was confirmed that the radiomics models with significant findings and challenges encountered in utilization of morphometric features. In the early detection and treatment of cancer, the morphometric evaluation is essential. To apply such features in practice while treating the patients, it is necessary to understand the usefulness, robustness, and problematic areas with respect to morphometric features.

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