A Methodology based on Formal Methods for Thermal Ablation Area Detection

Luca Brunese, Francesco Mercaldo, Antonella Santone and Giuseppe Peter Vanoli
Department of Medicine and Health Sciences "Vincenzo Tiberio", University of Molise, Campobasso, Italy

Keywords: Formal Methods, Thermal Ablation, Model Checking.

Abstract: Thermal ablation is the process related to the destruction of tissue by elevated tissue temperatures or depressed tissue temperatures. The machine exploited to perform for this process is named thermal ablator, requiring in input the area of the tissue to be subjected to treatment. In this proposal, with the aim to assist doctors in the process of the detection of the area targeted by the thermal ablator, we propose a methodology based on formal methods considering the representation of medical images in terms of formal and mathematical representations for the detection of the area.

1 INTRODUCTION AND BACKGROUND

The thermal ablation is defined as a needle-based treatment finalized to destroy cancerous or not normal tissue. There are two main ablation methods i.e., the extreme cold (also known as cryoablation) and the extreme heat (also known as radiofrequency or microwave ablation) (Choi and Jung, 2020).

The focus of thermal ablation is the cancer tissue destruction considering the generation of cytotoxic temperatures for a really short time-window in a not invasive way, clearly without damaging vital structures adjacent to the cancerous area. Typically considered techniques to perform the thermal ablation procedure for destroying tissue by elevating the tissue temperature above 55°C in the cancerous area include radiofrequency, microwave, ultrasound, and also laser ablation (Hegedüs et al., 2020). The cryoablation, from the other side, considers subzero temperatures to selectively freeze with the aim to destroy (only) the cancerous tissue. The innovation represents by both these ablative procedures is that they provide a minimal (e.g. percutaneously or laparoscopically) or non-invasive approach to the tumour therapy (Zhang et al., 2020).

The damage of the tissue can be controlled in an accurate way by considering a range of focused ultrasound transducers with different sonication sizes. In this context, medical images (for instance, magnetic resonance and computed tomography) allows the experts to continuously monitor the temperature rise in real time, allowing also in real-time the quantification of the dose of the therapy.

From the other side, ultrasound imaging and technique for the characterization of the tissue (for instance, elastography) can be exploited for monitoring the treatment relating to several clinical applications. Depending on the equipment and parameters considered, the volume of focused ultrasound lesions can be as small as a grain of rice (i.e., 10 cubic millimeters) (Song et al., 2013). This allows for an extremely localized treatment and a sharp border between treated and untreated areas.

For treatment of larger structures, as for instance tumors, multiple lesions can be combined in order to contain the full volume (Uchida et al., 2012; Song et al., 2013) of the cancerous area. A cooling period between different sonications is typically considered with the aim to reduce hte possibility of unwanted heating of surrounding tissue. This is the reason way, the treatment of really large tissue structures can be time-consuming. Anyway, optimized scanning algorithms, the injection of microbubbles aimed to increase the absorption of acoustic energy, and the adoption of spiral sonications are techniques currently exploited ofr the reduction of the treatments time (Brunese et al., 2019b).

The treatments exploiting thermal ablation are obtaining an increasing attention, as a matter of fact are considered an alternative to classic invasive surgical therapies, with particular regards to patients with contraindications or those who refuse open surgery (De Baere and Deschamps, 2014).

Brunese, L., Mercaldo, F., Santone, A. and Vanoli, G.
A Methodology based on Formal Methods for Thermal Ablation Area Detection.
DOI: 10.5220/0010394801910194
In *Proceedings of the 14th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2021) - Volume 3: BIOINFORMATICS*, pages 191-194
ISBN: 978-989-758-490-9

Today, thermal ablation is exploited in clinical applications with particular regard for kidney treating, prostate and others non-operable liver tumors. In this direction there is also an increasing application of thermal ablation techniques related to other organ sites including the brain (Brunese et al., 2020c), prostate, breast, lung, pancreas, thyroid and bone, symptomatic uterine fibroids; tumors in the prostate (Blana et al., 2004; Brunese et al., 2020f), breast, low back pain and brain disorders such as essential tremor, disease of Parkinson and neuropathic pain. The potential benefits of thermal ablation therapy are including reduced morbidity but also mortality in comparison with standard surgical resection and the ability to treat patients who are not surgical candidates (Thanos et al., 2004).

Even researchers have demonstrated that thermal ablation represents a successful technique for reduce tumours surface with minimal thermal damage to surrounding healthy tissue(Sajjadi et al., 2011), this technique requires expert pathologist and radiologist to localise the cancer area target of the thermal ablation (Baisi et al., 2013; Morgan et al., 2010; Raveglia et al.,).

Starting from these considerations, in this paper we introduce a proposal for a methodology based on formal methods for the automatic detection of the cancer area subjected to thermal ablation.

2 MODEL CHECKING FOR THERMAL ABLATION AREA DETECTION

In Figure 1 we show the flowchart related to our proposal.

We start from the analysis of medical images, that we convert into numerical values by exploiting radiomics i.e., a method that extracts a large number of features from radiographic medical images using data-characterisation algorithms (Brunese et al., 2020d; Brunese et al., 2020b; Iadarola et al., 2020; Brunese et al., 2020a).

We consider radiomics since it has been shown that it is able to exhibit disease characteristics that the naked eye fails (Brunese et al., 2020a).

In detail, we exploit different radiomic features belonging to five different categories (Van Griethuysen et al., 2017):

- *First Order*: this category describes the distribution of voxel intensities within the ROI (i.e., the region of interest, in this study related to the areas in the MRI interested by the cancer);
- *Shape*: this feature category includes descriptors of the three-dimensional size and shape of the ROI. These features are independent from the gray level intensity distribution in the ROI and are therefore only calculated on the non-derived image and mask;
- *Gray Level Co-occurrence Matrix* (GLCM): this category considers the spatial relationship of pixels is the gray-level co-occurrence matrix i.e., the gray-level spatial dependence matrix. The GLCM functions characterize the texture of an image by computing how often pairs of pixel with specific values and in a specified spatial relationship occur in an image and then extracting statistical measures from this matrix;
- *Gray Level Run Length Matrix* (GLRLM): the grey-level run length matrix (GLRLM) gives the size of homogeneous runs for each grey level. It quantifies gray level runs, which are defined as the length in number of pixels, of consecutive pixels that have the same gray level value;
- *Gray Level Size Zone Matrix* (GLSZM): the features belonging to this category quantify gray level zones in an image. A gray level zone is defined as the number of connected voxels that share the same gray level intensity. A voxel is considered connected if the distance is 1 according to the infinity norm.

The radiomic feature set obtained from each medical image related to the patient under analysis, is then translated into a formal model by exploiting the Calculus of Communicating Systems (Milner, 1989). To detect the area of the thermal ablation on the formal model (Casolare et al., 2019; Casolare et al., 2020), we need a set of properties expressed in a temporal logic, for instance, in the mu-calculus logic (Stirling, 1989), describing the cancerous area subjected to thermal ablation. The properties are formulated with the knowledge of expert radiologists and pathologists. In details, our proposal considers several properties, each one related to a particular area of the medical image. For example, if we ideally divide the medical image into four equal parts, we will define four properties, each one relating to one of the four areas. Once obtained the formal model and the related properties, we invoke a formal verification environment (for instance, the CWB-NC[1]) to verify if the thermal ablation area properties are satisfied by the formal model obtained from the medical images.

When the formal verification environment outputs *TRUE* on a certain property, the formal model will

[1] https://www3.cs.stonybrook.edu/~cwb/

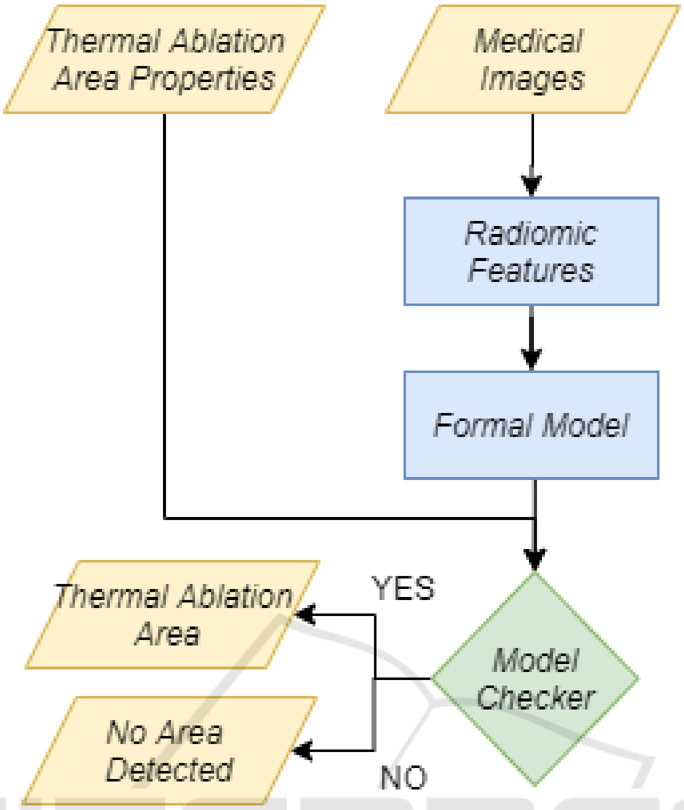

Figure 1: The flowchart.

exhibit the area subjected to thermal ablation in the zone identified by the formula. Otherwise, the formal verification environment outputs *FALSE* meaning that the formal model will not exhibit an area subjected to thermal ablation in the zone identified by the formula (Iadarola et al., 2019; Brunese et al., 2020e; Brunese et al., 2019a).

3 CONCLUSION AND FUTURE WORK

The thermal ablation technique is typically used for patients with unresectable and borderline resectable disease, which may be due to the size, number or location of the tumors, or for patients judged inoperable due to the poor helath of the patient. This technique requires the aid of radiologists and pathologists to exactly localise the tumour area object of the thermal ablation. In this paper, we propose a method to localise the cancerous area subjected to the thermal ablation therapy by exploiting medical image analysis. In details, we consider radiomics features to obtain numerical values from medical images, and model checking, to automatically detect the area for the thermal ablation application. As future works, we plan to specify the temporal logic properties for the automatic area detection. Moreover, it will be of interest to understand whether the automatic area detection properties rightly work on different type on organ. Moreover, we plan to apply also deep techniques in order to understand the results. We plan to apply an architecture based on Convolution Neural Network, typically exploited for processing visual data and 2D data. Basically, a CNN is made up of one or more convolutional layers with fully connected upward layers. It also consider common weights and layers (i.e., pooling layers). In particular, ”max-pooling” is often used in Fukushima’s convolutional architecture (Deng et al., 2014), allowing CNNs to take advantage of 2D input structures. As a matter of fact, they are particularly effective in the area of images and speech recognition.

REFERENCES

Baisi, A., De Simone, M., Raveglia, F., and Cioffi, U. (2013). Thermal ablation in the treatment of lung cancer: present and future. *European Journal of Cardio-Thoracic Surgery*, 43(4):683–686.

Blana, A., Walter, B., Rogenhofer, S., and Wieland, W. F. (2004). High-intensity focused ultrasound for the treatment of localized prostate cancer: 5-year experience. *Urology*, 63(2):297–300.

Brunese, L., Martinelli, F., Mercaldo, F., and Santone, A. (2020a). Deep learning for heart disease detection through cardiac sounds. *Procedia Computer Science*, 176:2202–2211.

Brunese, L., Martinelli, F., Mercaldo, F., and Santone, A. (2020b). Machine learning for coronavirus covid-19 detection from chest x-rays. *Procedia Computer Science*, 176:2212–2221.

Brunese, L., Mercaldo, F., Reginelli, A., and Santone, A. (2019a). Formal methods for prostate cancer gleason score and treatment prediction using radiomic biomarkers. *Magnetic resonance imaging*.

Brunese, L., Mercaldo, F., Reginelli, A., and Santone, A. (2019b). Radiomic features for medical images tamper detection by equivalence checking. *Procedia Computer Science*, 159:1795–1802.

Brunese, L., Mercaldo, F., Reginelli, A., and Santone, A. (2020c). An ensemble learning approach for brain cancer detection exploiting radiomic features. *Computer methods and programs in biomedicine*, 185:105134.

Brunese, L., Mercaldo, F., Reginelli, A., and Santone, A. (2020d). Explainable deep learning for pulmonary disease and coronavirus covid-19 detection from x-rays. *Computer Methods and Programs in Biomedicine*, 196:105608.

Brunese, L., Mercaldo, F., Reginelli, A., and Santone, A. (2020e). Formal methods for prostate cancer gleason score and treatment prediction using radiomic biomarkers. *Magnetic resonance imaging*, 66:165–175.

Brunese, L., Mercaldo, F., Reginelli, A., and Santone, A. (2020f). Radiomics for gleason score detection through deep learning. *Sensors*, 20(18):5411.

Casolare, R., Martinelli, F., Mercaldo, F., and Santone, A. (2019). A model checking based proposal for mobile colluding attack detection. In *2019 IEEE International Conference on Big Data (Big Data)*, pages 5998–6000. IEEE.

Casolare, R., Martinelli, F., Mercaldo, F., and Santone, A. (2020). Malicious collusion detection in mobile environment by means of model checking. In *2020 International Joint Conference on Neural Networks (IJCNN)*, pages 1–6. IEEE.

Choi, Y. and Jung, S.-L. (2020). Efficacy and safety of thermal ablation techniques for the treatment of primary papillary thyroid microcarcinoma: a systematic review and meta-analysis. *Thyroid*, 30(5):720–731.

De Baere, T. and Deschamps, F. (2014). New tumor ablation techniques for cancer treatment (microwave, electroporation). *Diagnostic and interventional imaging*, 95(7-8):677–682.

Deng, L., Yu, D., et al. (2014). Deep learning: methods and applications. *Foundations and Trends® in Signal Processing*, 7(3–4):197–387.

Hegedüs, L., Miyauchi, A., and Tuttle, R. M. (2020). Nonsurgical thermal ablation of thyroid nodules: Not if, but why, when, and how? *Thyroid*.

Iadarola, G., Martinelli, F., Mercaldo, F., and Santone, A. (2019). Formal methods for android banking malware analysis and detection. In *2019 Sixth International Conference on Internet of Things: Systems, Management and Security (IOTSMS)*, pages 331–336. IEEE.

Iadarola, G., Martinelli, F., Mercaldo, F., and Santone, A. (2020). Image-based malware family detection: An assessment between feature extraction and classification techniques. In *IoTBDS*, pages 499–506.

Milner, R. (1989). *Communication and concurrency*. PHI Series in computer science. Prentice Hall.

Morgan, G. J., Clarke, K., Caldarone, C., and Benson, L. N. (2010). Radiolucent retractor for angiographic analysis during hybrid congenital cardiac procedures. *The Journal of thoracic and cardiovascular surgery*, 140(5):1195–1196.

Raveglia, F., Rizzi, A., De Simone, M., Cioffi, U., Sacrini, A., and Baisi, A. State of the art in alternative treatments for lung cancer: Thermal ablation therapy.

Sajjadi, A. Y., Mitra, K., and Grace, M. (2011). Ablation of subsurface tumors using an ultra-short pulse laser. *Optics and Lasers in Engineering*, 49(3):451–456.

Song, J. H., Yoo, Y., Song, T.-K., and Chang, J. H. (2013). Real-time monitoring of hifu treatment using pulse inversion. *Physics in Medicine & Biology*, 58(15):5333.

Stirling, C. (1989). An introduction to modal and temporal logics for ccs. In Yonezawa, A. and Ito, T., editors, *Concurrency: Theory, Language, And Architecture*, volume 491 of *LNCS*, pages 2–20. Springer.

Thanos, L., Mylona, S., Pomoni, M., Kalioras, V., Zoganas, L., and Batakis, N. (2004). Primary lung cancer: treatment with radio-frequency thermal ablation. *European radiology*, 14(5):897–901.

Uchida, T., Nakano, M., Hongo, S., Shoji, S., Nagata, Y., Satoh, T., Baba, S., Usui, Y., and Terachi, T. (2012). High-intensity focused ultrasound therapy for prostate cancer. *International Journal of Urology*, 19(3):187–201.

Van Griethuysen, J. J., Fedorov, A., Parmar, C., Hosny, A., Aucoin, N., Narayan, V., Beets-Tan, R. G., Fillion-Robin, J.-C., Pieper, S., and Aerts, H. J. (2017). Computational radiomics system to decode the radiographic phenotype. *Cancer research*, 77(21):e104–e107.

Zhang, T., Liang, W., Song, Y., Wang, Z., and Zhang, D. (2020). Us-ct fusion image-guided microwave ablation of lung cancer—-a new mode of image guidance in lung cancer ablation. *ADVANCED ULTRASOUND IN DIAGNOSIS AND THERAPY*, 4(4):343–348.