Seminar Paper Critical Review:
Consensus Recommendations for Radiation Therapy Contouring and Treatment of Vulvar Carcinoma

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2 Introduction:

2.1 Project Overview

My project is the Anomaly Detection for Treatment Planning and a Learning Health System in Radiotherapy. The main purpose of the project is to build the framework for a modular software that will allow clinicians and physicians to test the integrity of their contour models in an automated and systematic fashion. We hope that by building the foundations for such software, we can improve the quality of existing and future clinical data via an active approach. The secondary goal of the project is to design and test our own integrity checks. We hope to identify potentially erroneous data with various statistical anomaly detection methods with high accuracy. By developing various automated methods, we want to determine the various features that would allow us to select images with high accuracy contour confidence or with anomalous results.

2.2 Paper selection

One of the final overarching goals for our project is assessing image quality to determine anomalous data. There are several previous studies that approach this in a manual fashion, contrasting the autonomous design of our project. I choose a paper that looked at one such manual version of what we want to develop. Instead of an automated integrity checker, the paper had various expert gynecologic radiation oncologists perform a survey to create a set of recommendations; then, 14 physicians contoured two cases. The goal was to develop a radiation therapy contouring atlas for woman with vulvar carcinoma to generate a standardized set of recommendations to approach vulvar cancer radiation therapy.

2.3 Key Contributions and Results

The key result was that expert oncologists were able to generate a set of consensus recommendations for contouring target volumes and treatment for vulvar cancer. However, due to lack of clinical research evidence, the study also advocates to use a conservative and consistent approach and to tailor treatment to suit the individual needs of patients.

3 Background:

3.1 Vulvar Cancer

Vulvar cancer is a type of outer surface gynecologic neoplasm. This means it is an abnormal growth of tissue on the outer surface of the female genital organs. 95% of the cases are squamous cell carcinoma, which means it arises from the epithelium (squamous) cells. It is relatively rare, with <20,000 US cases per year, thus accounting for about 5% of gynecologic malignancies. Generally, vulvar cancer occurs in older post-menopausal women, but over the last 20 years, there has been a rise in the number of cases in premenopausal women as well. Vulvar cancer is caused by various factors such as HPV and lichen sclerosis. It primarily occurs on the labia majora, labia minora, clitoris, and perineum.

3.2 Radiation Therapy (RT)

Radiation therapy is a type of curative treatment that involves using high energy waves, such as x-rays, to damage and kill cancer cells. The radiation source can be both internal and external. Internal radiation therapy is when a radioactive source is placed inside of the body. External radiation therapy are when high energy waves are directed at a target location from outside the body. 35% of cancer patients will have radiotherapy as some part of their primary treatments.

In the proximity of the vulva and groin area, there are several sensitive organs at risk (OARs). Combined with the steep changes in the source-to-skin distance in the area, vulvar cancer is difficult to treat with 3-dimensional (3D) RT. There are some existing methods to improve avoidance of critical structures, such intensity modulated RT (IMRT), which involves using computer controlled linear accelerators to precisely deliver radiation doses.

4 Methodology

4.1 Initial Recommendations

In order to establish the initial contour recommendations, a survey was conducted among expert radiation oncologists. A total of 35 physicians completed the survey. Using the data collected, areas of clinical controversy were identified and discussed over several meetings. From this information, an initial draft for the consensus contouring recommendations was generated.

4.2 Case Studies

After the initial draft was finalized, committee members were invited contour 2 cases. They were given explicit instructions and the initial diagnostic positron emission tomography (PET)/computed tomography (CT) images. The instructions stated that the physicians had to contour both the vulvar and nodal clinical tumor volumes as a single structure based on the initial recommendations from the survey. The resulting contours were then submitted for analysis.

4.3 Refined Recommendations

Once the results were received, a 95% confidence interval contour was developed from the contours from each case, using Computerized Environment for Radiation Research (CERR) software. Using an expectation-maximization algorithm for simultaneous truth and performance level estimation (STAPLE), the contours were compared and analyzed. STAPLE allowed for the identification of a consensus segmentation. The level of agreement between contours was assessed by a kappa statistic, which measures the inter-rater agreement for qualitative items. Certain important values, such as the conformity indices were calculated. The outlined contours were then edited using MIM software and presented to the committee.

4.4 Further refinement

After generating the 95% confidence contour using CERR, the committee did multiple reviews in order to determine how the model should be improved. It was determined that the consensus contour was too close to the skin in select locations and retracted in order to avoid skin toxicity in low risk areas. Similarly, other low risk areas were removed, such as the lateral to femoral vessels and tissue posterior. However, it is noted that these should be removed with care and added back in for certain patients. Further refinement was done until all contributing authors were satisfied with the safety and comprehensiveness of the recommendations.

5 Results

The initial survey of oncologists demonstrated that the gynecologic region can be divided into areas of agreement and areas of controversy. Areas of greatest agreement were inclusion of vulvar, inguinal, and pelvic nodes. Areas of initial controversy included delineation and inclusion of the "skin bridge," the width of the inguinal contour, the inclusion of skin above the inguinal nodes, and the superior border of the pelvic nodes. After initial survey data was collected and consensus was reached, the initial contour recommendations were passed to the clinicians to do case studies. The results of the 14 contours following the recommendations showed a high level of agreement, with kappa statistics of 0.69 and 0.64 for cases 1 and 2. Using these contours, a specificity of 99.0% was reached for both cases. The sensitivity was 71.3% and 64.9% for cases 1 and 2. What the high specificity and moderate sensitivity indicates is that the physicians had higher confidence in which structures to exclude compared to which structures to include from the CTV. After editing the contour using MIM, the committee then refined the 95% confidence intervals and individual contours. The committee also refined the recommendations for the contouring. The actual guidelines are listed in the paper after the results section. Note that the authors specify that the 3-dimensional structure of a vulvar CTV is very complex so physicians should exercise caution and care when contouring the region. The authors also realize that there is little clinical research evidence supporting their recommendations, so the committee advocates using a conservative and consistent approach to using the recommendations.

6 Assessment

6.1 Pros

- Clear explanation of recommendation generating process that included several refinement steps.
- Realizes lack of clinical validation is a weakness, warns against solely using recommendations.
- Clear images, tables, and figures demonstrating results.
- Included guidelines at the end.

6.2 Cons

- Results show that the consensus recommendations only had moderate sensitivity, which means that rate of identifying patients with the disease is not perfect

- The lack of clinical research evidence to support the study makes it so that the recommendations are less trustworthy.
- The study only did two cases to refine recommendations. These were two general cases, but more cases could have helped make the recommendations clearer. Also, there were only 14 contours per case, which can be affected by the variation between individuals.

6.3 Relevance

The study demonstrates how to generate manual guidelines for contour recommendations. It also determines the specificity and sensitivity of such recommendations. It completes integrity checking in radiation therapy over a given set of patients. Similarly, our project involves generating automated guideline modules based on the needs of the user. We can then calculate the specificity and sensitivity of different modules. There is a lot of manual labor involved in the process described in the study. We want to be able to remove these human aspects, which can be subject to error, and implement an active computational approach to improving integrity. Our framework will take similar instructions in, run it across a large clinical database, and determine the similar recommendations. We will be able to detect anomalous anatomy and report it to the clinician without having to go through an extensive review.

7 Conclusion

The final conclusion is that this paper is useful helping us understand the current workflow of generating consensus recommendations for contouring various regions of the body. It demonstrates how the process works and areas that can be automated. The paper also provides several interesting points that we need to consider in our own design, such as specificity versus sensitivity, and large clinical support for our results. There are also some possible directions for modules we can design, such as organ volume, as well as understanding some of the mechanics behind detecting agreement between contours. All together, the paper really demonstrated the need for our project in order to increase the efficiency of radiation oncology.