

A KNOWLEDGE BASED AUTOMATIC RADIATION TREATMENT PLAN ALERT SYSTEM

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ABSTRACT

In radiation therapy, preventing treatment plan errors is of paramount importance. In this paper, an alert system is proposed and developed for checking if the pending cancer treatment plan is consistent with the intended use. A key step in the development of the paper is characterization of various treatment plan fingerprints by three-dimension vectors taken from possibly thousands of variables in each treatment plan. Then three machine learning based algorithms are developed and tested in the paper. The first algorithm is a knowledge-based support vector machine method. If an incorrect treatment plan were offered, the algorithm would tell that the pending treatment plan is inconsistent with the intended use and provide a red flag. The algorithm is tested on the actual patient data sets with 100% successful rate and 0% failure rate. In addition, two algorithms based on the well-known k-nearest neighbour and Bayesian approach respectively are developed. Similar to the support vector machine algorithm, these two algorithms are also tested with 100% success rate and 0% failure rate. The key seems to pick up the right features.

KEYWORDS

Oncology, radiation safety, cancer treatment plans, machine learning, radiation error detection

1. INTRODUCTION

Americans today receive far more medical radiation than ever before: the average lifetime dose of diagnostic radiation has increased seven-fold since 1980 [1]. Half of all cancer patients receive some types of radiation therapy sometime during the course of their treatment [2]. Radiation therapy has seen significant technological advancements in the last fifteen years [3], and at the same time, its complexity has created many sources of errors, such as software flaws, faulty programming, poor safety procedures, or inadequate staffing and training [1]. The growing dependence on technology (e.g., more automated computer systems and software interlocks for the design of radiation plans and the treatment delivery) and increases in treatment plan complexity often makes it impossible for any individual to independently verify that the treatment is delivered exactly as intended [4]. The lack of adequate alert systems when a treatment has gone wrong has been cited as a significant factor that can impact patient safety [4] in radiation therapy.

Treatment errors in radiation oncology occur at a rate of 2% per patient [5] approximately 16,000 patients/year, and this rate may be under-reported [8]. For instance, a patient with bilateral trigeminal neuralgia was to have treatment on 1 side, but the prescription and plan were both done for the other side. The wrong treatment was only prevented when the therapist asked the patient which side was to be treated [9]. There are no comprehensive numbers available for the

number of radiation errors resulting in death [10]. Providers may fail to report events for many reasons, including the fear of publicity or punitive actions (e.g., lawsuits), lack of knowledge of the event, or misunderstandings about the reporting system [12]. Regulators and researchers can only guess how often radiotherapy adverse events occur. With no single agency overseeing medical radiation, there is no central clearinghouse for reporting, and twenty-three states do not require that adverse events be reported at all [8].

The trend toward using more sophisticated and technologically complex equipment and procedures in radiation oncology requires additional safeguards to improve patient safety [15]. It also provides opportunities for innovation. A survey of radiation oncology professionals [16] shows that any technology solution must meet the requirements for cost efficiencies and time efficiency. High workloads were reported as the biggest challenge cited by the highest number of medical physicists surveyed. Radiation therapy's complexity is expected to increase in the next few years, but survey participants cited high workloads as a factor that slows the speed of adopting new technology: they picked faster quality assurance per patient as the main opportunity for near future development. Preventing treatment errors involves identifying two types of data aberrations: incorrect chart data (patient specific error) and unusual chart data (class-specific error). In radiotherapy, patients are positioned on a treatment couch in order to move the tumor into the radiation beam. This is performed for an entire course of treatment, with one treatment fraction delivered each day for several weeks. Reproducibility of patient setup is extremely important. An inconsistent treatment couch position for a patient is an example of a patient specific error. If the maximum difference between the actual treatment couch position and the planned treatment couch position is 2 mm in the first ten fractions, a 10 mm difference in the couch position at the 11th fraction would be identified as a potential patient-specific error. For class-specific errors, the data for a given patient may be noticeably different from the data for a similar group of patients. For example, if the treatment couch position for left breast cancer patients is always positive on the couch coordinate system, a negative treatment couch position for a left breast cancer patient would be unusual. To find these errors in radiation therapy, medical physicists manually review treatment charts [17]. This manual reviewing process relies heavily on the experience of the radiation therapy team – especially for detecting class-specific problems. Moreover, due to resource limitations, chart-checking may not be performed as often as needed. The minimum recommended frequency is weekly [18], but this process varies among institutions. Some check on a fixed day, which makes the distribution of intervals between subsequent checks suboptimal, or they try to check daily, but waste time opening ineligible charts [19]. When chart-checks are performed only once a week, it is more likely that a serious error will not be caught in time to prevent significant patient harm [20].

Current radiation oncology information systems (ROIS) gather the data to be checked for a requested patient and display the data on a computer screen. While these ROIS make the chart-check process more convenient, it does not automate the process of error detection. ROIS does not provide tools to find class-specific problems and identify unusual conditions. Hence, checking charts for a large number of patients is challenging [21] and inefficient, and errors are too often overlooked; moreover, all chartchecks are performed retrospectively – i.e., medical physicists can only review the treatment charts after the treatment is delivered. We propose to develop a machine learning based automated real-time prospective chart-checking system to improve chart-checking efficiency by offloading repetitive tasks to computers, with the goal of reducing human error. A critical advantage of analyzing real-time treatment data is that it enables performance of prospective error detection, potentially preventing treatment errors before treatment starts. It will not only flag abnormal treatments, but also provide clinical benchmarks to improve the safety and efficiency of radiation treatments. Manual checks still prevail in most radiation oncology departments because it is a complex task to build, adapt, and test chart-checking software for automating specific combinations of continually evolving platforms and modalities [22] for

radiation treatment. Our proposed method is to address this technology challenge of customization and adaption to the individual clinic. It will improve clinical practice in radiation therapy by significantly increasing the accuracy, effectiveness, and efficiency of chart-checking. We make a remark here. The study report in this paper was focused on the data set collected from an institution. However, the technique can be generalized to address the customization to the individual clinics.

The system we propose to develop will perform treatment plan analysis before treatment starts. As soon as it detects a problem, the system can alert users to take action. First, a support vector machine (SVM) based algorithm is to be developed to detect abnormal treatment plans. Current in house chartchecking software lacks the ability to understand and abstract the inherent pattern of specific radiation therapy treatment plans. A machine learning (ML)-based algorithm would learn and understand the inherent treatment patterns from clinical radiation therapy treatment plans. The idea is not new. In [13], a cluster method was proposed with eight variables: beam energies and monitor units (MUs) for the four radiation fields. However the study was limited to a specific cancer treatment plan, prostate cancer treatment plan only. Also in [14], a way to detect data errors in treatment plans was proposed. The goal is again to detect treatment parameter errors for a given treatment plan but not to make distinguishable of treatment plans for different types of cancer. Our goal in this paper is to design a ML-based algorithm that can automatically detect if a pending treatment plan is consistent with the intended type of cancer treatment. The algorithm is tested on the actual patient data sets with 100% successful rate and 0% failure rate. Further, two algorithms based on the well known K-nearest neighbor and Bayesian methods respectively are also developed. In the Bayesian approach, prior information is exploited and incorporated into the algorithm. Both algorithms are tested on actual patient data sets with 100% successful rate and 0% failure rate. It is interesting to observe, as expected, that the choice of treatment plan fingerprints is critical. Once the right fingerprints are selected, choice of which machine learning algorithm seems less important.

The layout of the paper is as follows: Data collection and features selection are discussed in Section. Section 3 focuses on classification by Support Vector Machine (SVM). In addition, K-nearest neighbor and Bayesian approach are also applied in Sections 4-5 respectively. Section 6 provides some remarks as well as further research directions.

2. DATA AND FINGERPRINTS SELECTION

In the proposed study, the treatment plans from a cohort of head-neck cancer, breast cancer, and prostate cancer were investigated. Radiation therapy treatment follows patterns and different cancer treatment plans have distinct characteristics, or "fingerprints". With machine learning and pattern recognition techniques, it is expected that the algorithm will learn the specific "fingerprints" from previous treatment plans and build the knowledge base for each specific cancer treatment plans. The ML-based treatment plan analysis and error detection will enable algorithms to perform "smart" checks beyond simple number or name comparison. Once the "fingerprints" of each treatment are created, the system can alert users of inappropriate treatment plans and potentially prevent adverse treatment events. For example, the ML-based system can distinguish between a breast cancer treatment plan and a prostate treatment plan. Such intelligent algorithms could save patient's life by alerting users of inappropriate and dangerous treatments [1].

The first and probably the most difficult question is what constitutes fingerprints for a particular treatment plan. Fingerprints must be unique and are readily distinguishable from fingerprints of other treatment plans. Note in each treatment plan, there are thousands of variables. Practically, computation on thousands of variables is not preferable. The goal is to find a few variables or a

few variables that are functions of those thousands of original variables. These a few variables or a few variables that are functions of those thousands of variables form fingerprints. Intuitively, three types of cancers have different shapes, volumes and the relative locations of treatment. Now the question is how to capture these intuitive but hard to describe characteristics. Recall in a radiotherapy machine, the gantry moves a radiation source around a patient. A linear accelerator is built into the top part of the gantry. The gantry is supported by a drive stand, which rotates the gantry on a fixed horizontal axis as the linear accelerator revolves around a patient. An beam generator in the drive stand behind the gantry supplies radio frequency energy to the linear accelerator. Shaped beam radio surgery uses a multi-leaf collimator made up of mechanical parts called leaves. The leaves move separately, programmed in the planning process to precisely match the shape of the treatment beam to the shape of the tumor. Tumors are rarely perfectly shaped, so the multi-leaf collimator can be adjusted to fit the shape of the tumor, allowing the maximum dose of radiation to be evenly distributed to the entire tumor and the minimum dose of radiation to neighboring organs. Figure 1 demonstrates a radiation oncology system that include an accelerator, gantry and multi-leaves collimator.

Actual radiation treatment plans of head-neck, prostate and breast cancers are collected at the University of Iowa Hospital and Clinic. Let $P(i, j)$ be the position value of the i th leaf at the j th gantry angle. Let N_L and N_G represent the total numbers of the leaves (=80) and gantry angles (depending on treatment plans). Figures 2-4 show $P(i, j)$ for three different cancer treatment plans. It is observed that the variations along both the leaf number and the gantry angle direction were larger for the head-neck plans and much smaller for the prostate plans. For breast treatment plans, the variations along both directions were large but the variation for a fixed gantry angle was much larger.

Therefore in spite of thousands of variables in treatment plans, the averages of variations along the leaf number and gantry angle directions respectively served well as two fingerprints of the treatment plan validation. More precisely at j th gantry angle, define



Figure 1. Accelerator, gantry and collimator

$$P_L(j) = \frac{1}{N_L} \sum_{i=1}^{N_L} (P(i, j) - \mu_j)^2, j = 1, 2, \dots, N_G \quad 1$$

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and at i th leaf, define

$$P_G(i) = \frac{1}{N_G} \sum_{j=1}^{N_G} (P(i,j) - v_j)^2, i = 1, 2, \dots, N_L \quad 2$$

where

$$\mu_j = \frac{1}{N_L} \sum_{i=1}^{N_L} P(i,j), \quad v_j = \frac{1}{N_G} \sum_{i=1}^{N_G} P(i,j)$$

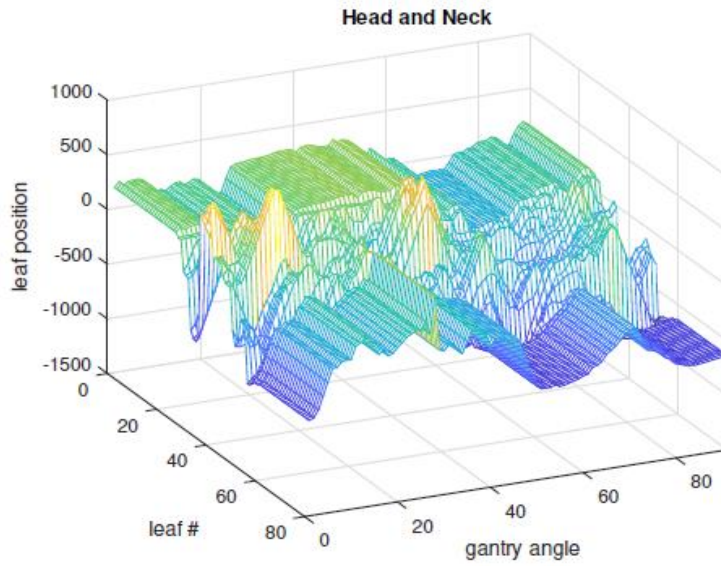


Figure 2. Variation in leaf position vs variation in gantry angle, head-neck cancer.

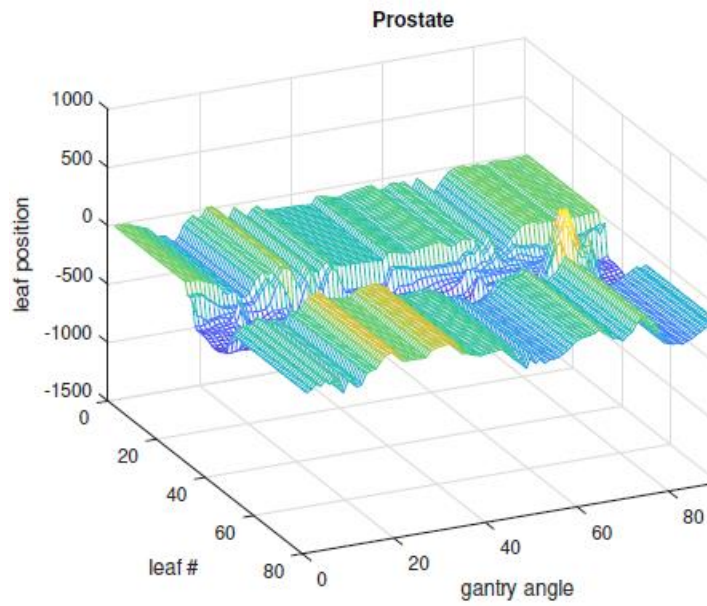


Figure 3. Variation in leaf position vs variation in gantry angle, prostate cancer.

Finally, define the average variations along the leaf and the gantry angle directions respectively,

$$P_{AL} = \frac{1}{N_G} \sum_{j=1}^{N_G} P_L(j), \quad P_{AG} = \frac{1}{N_L} \sum_{i=1}^{N_L} P_L(j), \quad 3$$

In addition, it is clear that the number of gantry control points of breast cancer treatments is much smaller than that of head-neck and prostate cancer treatments. This is definitely another fingerprint.

Fourteen treatment plans (five head-neck cancer, four prostate cancer, and five breast cancer) were collected. Figure 5 shows a three dimension diagram in terms of the average variations P_{AL} along the leaf position, the average variation P_{AG} along the gantry angle and the gantry control points of head-neck, prostate, and breast cancer treatment plans respectively. Clearly, three different treatment plans are separated and this provides the evidence that two variations plus the gantry control points form fingerprints in a 3-dimensional space. This is practically very important because of their separability and simplicity.

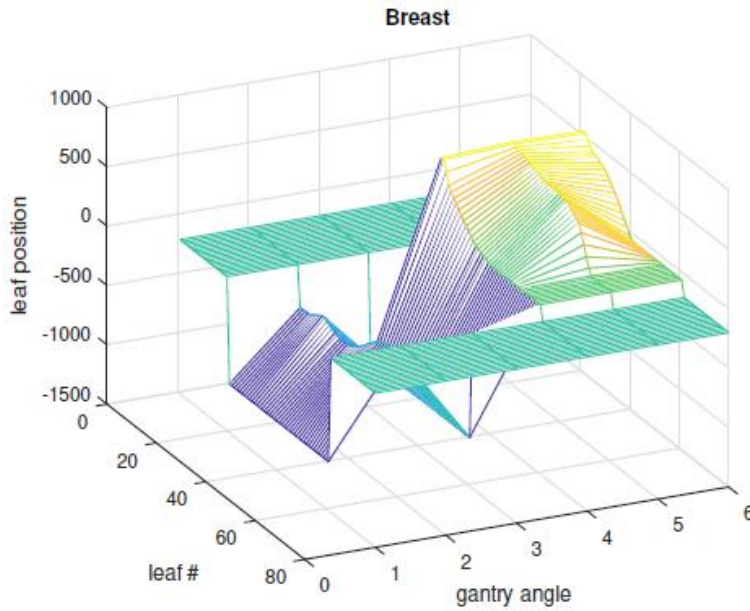


Figure 4. Variation in leaf position vs variation in gantry angle, breast cancer.

Since the proposed ML approach also works on the projection of this 3-dimensional space to 2-dimension spaces, projections of Figure 5 to three 2-dimensional spaces are shown in Figures, 6, 7 and 8. Figure 6 is the projection to the 2-dimensional space, variation-leaf position vs variation-gantry angle. Figure 7 is the projection to the 2-dimensional space, number of gantry control points vs variation gantry angle. Figure 8 is the projection to the 2-dimensional space, number of gantry control points vs variation-leaf position.

3. SUPPORT VECTOR MACHINE APPROACH

3.1. Algorithm development

Once fingerprints, the variation in the leaf position, the variation in the gantry angel and the number of gantry control points, are obtained, the next step is to develop a machine learning

algorithm to classify three different treatment plans. We choose the support vector machine (SVM) [23] because of its simplicity. However, a typical SVMs only deal with 2 classes. Our 3-class problem, we repeat SVM twice.

Since head-neck and prostate cancer treatments have similar numbers of gantry control points and breast cancer treatments have a much lower number of gantry control points, we group head-neck and prostate cancer treatments together as one group, and breast cancer treatments as a different group. Then we apply the first SVM as shown in the bottom diagram of Figure 9. Once breast cancer treatments are separated, we then apply SVM again for a 2-class problem, head-neck cancer treatments vs prostate cancer treatments as shown in the top diagram of Figure 9.

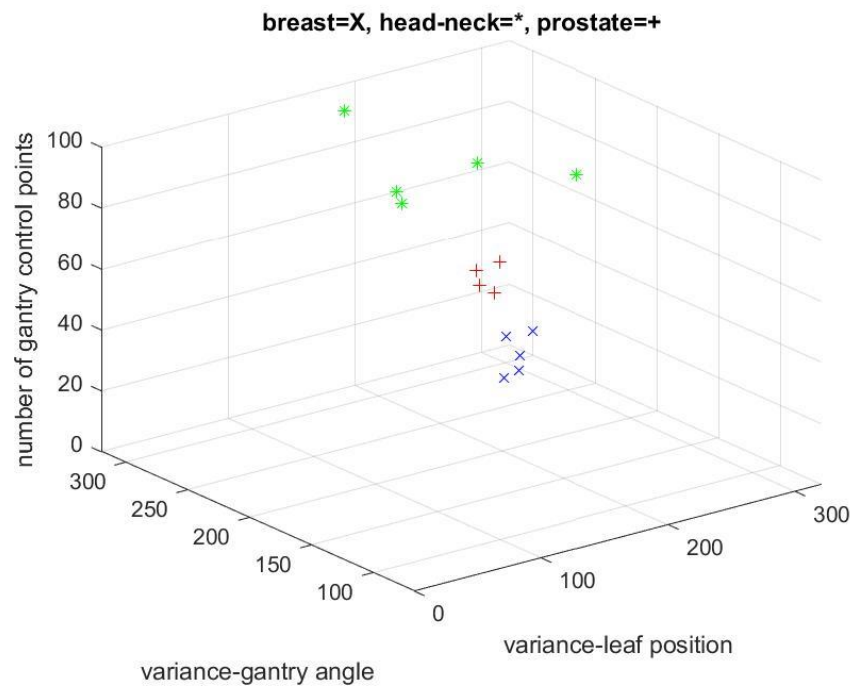


Figure 5. Variation in the leaf direction, variation in the gantry angle direction and the gantry control points for three different cancer treatment plans, +=prostate, *=head-neck X=breast.

3.2. Validation of SVM

To validate the proposed algorithm, 14 cancer treatment plans were collected at the University of Iowa Hospital and clinic, five head-neck cancer, four prostate cancer, and five breast cancer. For each test, 1 head-neck cancer data, 1 prostate cancer data and 1 breast cancer data were used as validation data and the remaining 4 head-neck cancer data, 4 breast cancer data and 3 prostate cancer data were used as training data. The classification model was calculated based on the training data only and no validation was known when the classification was carried out. Then, validation was tested on the three validation data: one head-neck, one breast and one prostate. A validation was successful if the three-class SVM constructed by the remaining 11 training sets can individually identify three validation data correctly.

Table 1. Successful and failure rates of 100 SVM validation

# of Tests	# of Success	# of Failure
100	100	100

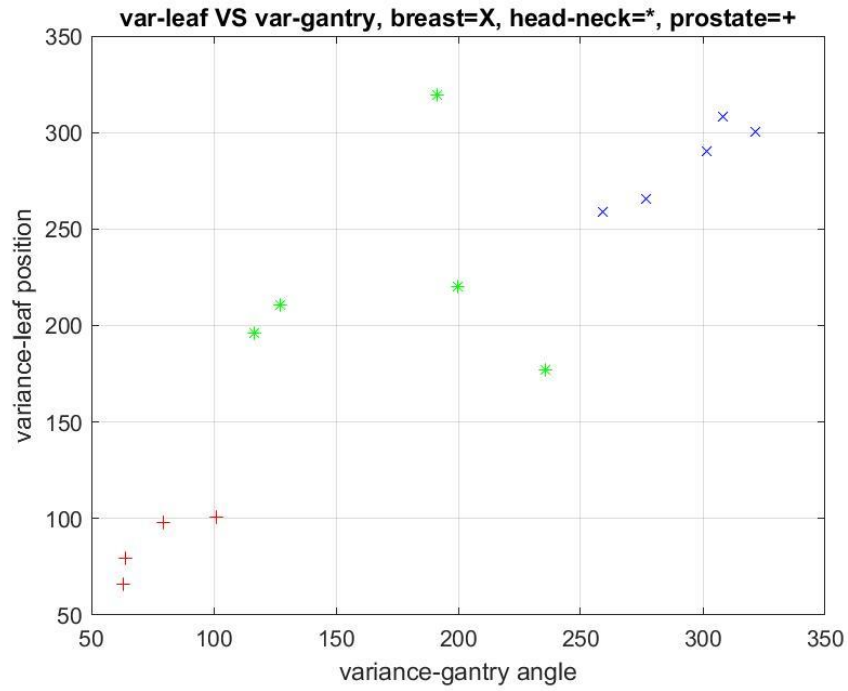


Figure 6. Variation in the leaf direction vs variation in the gantry angle direction for three different cancer treatment plans, +=prostate, *=head-neck X=breast.

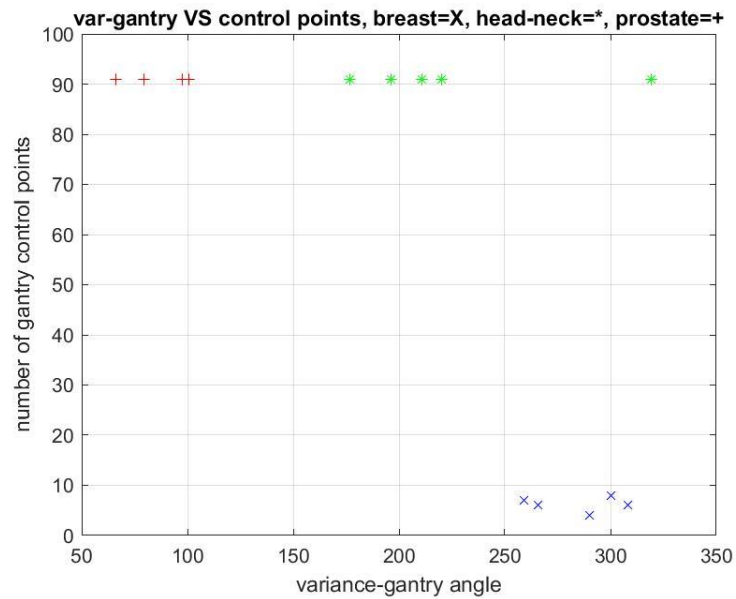


Figure 7. Gantry control points vs variation in the gantry angle direction for three different cancer treatment plans, +=prostate, *=head-neck, X=breast.

A validation was failed if any one of three validation data was misidentified. There were $5 \times 5 \times 4 = 100$ different combinations. Table 1 shows the results of 100 tests and the successful rate is 100%.

4. K-NEAREST NEIGHBOR APPROACH

The most important thing in this application is the dimension reduction/feature selection. Once the “right” features are selected, many machine learning algorithms work well. This and next sections illustrate this point by showing that both K-nearest neighbor and Bayesian approach work well based on the features selected. The idea of the K-nearest neighbour algorithm [6] is that data points of the same pattern stay in close proximity. Usually, it consists of the following steps.

1. Collect data including training and testing data sets.
2. Fix k , that is the chosen number of neighbors and define the distance. The available prior information should be incorporated into the definition.
3. For each testing point, calculate the distance between the testing data point and every training data point.
4. Sort the ordered distances and indices from smallest to largest by the distances.
5. Find the first k entries and their pattern labels from the list.
6. From the first k entries, determine the pattern of the testing point by the majority vote.

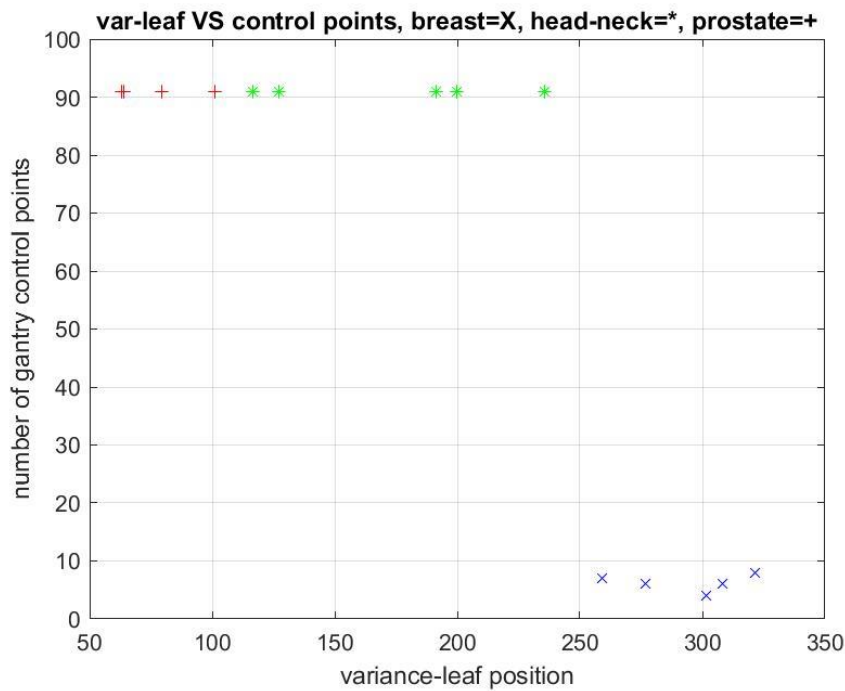


Figure 8. Gantry control points vs variation in the leaf direction for three different cancer treatment plans, +=prostate, *=head-neck X=breast.

In this application, the number of data points is limited, 5 breast cancer treatment plans, 5 head-neck cancer treatment plans and 4 prostate cancer treatment plans. For each test, 1 head-neck cancer data, 1 prostate cancer data and 1 breast cancer data were used as validation data and the remaining 4 head-neck cancer data, 4 breast cancer data and 3 prostate cancer data were used as training data. The maximum number of data points in each training sets is 3. Thus, $k=3$ makes perfect sense. Another critical factor in the K-nearest neighbor approach is the definition of the distance. The standard distance works well and achieves 100% successful rate in the test. On the other hand by a close look, it is noticed that all breast cancer treatments are far away from all head-neck and prostate cancer treatments in the vertical direction. To make the algorithm more

robust against contamination, we can and should scale down the vertical direction by defining the distance between two points as

$$d = \{(x_1(1) - x_2(1))^2 + (x_1(2) - x_2(2))^2 + (x_1(3) - x_2(3))^2 / w\}^{\frac{1}{2}}, \quad 4$$

for some $w > 0$ as a hyper parameter. It will be shown that the choice of w is not sensitive and any $w \geq 1$ works.

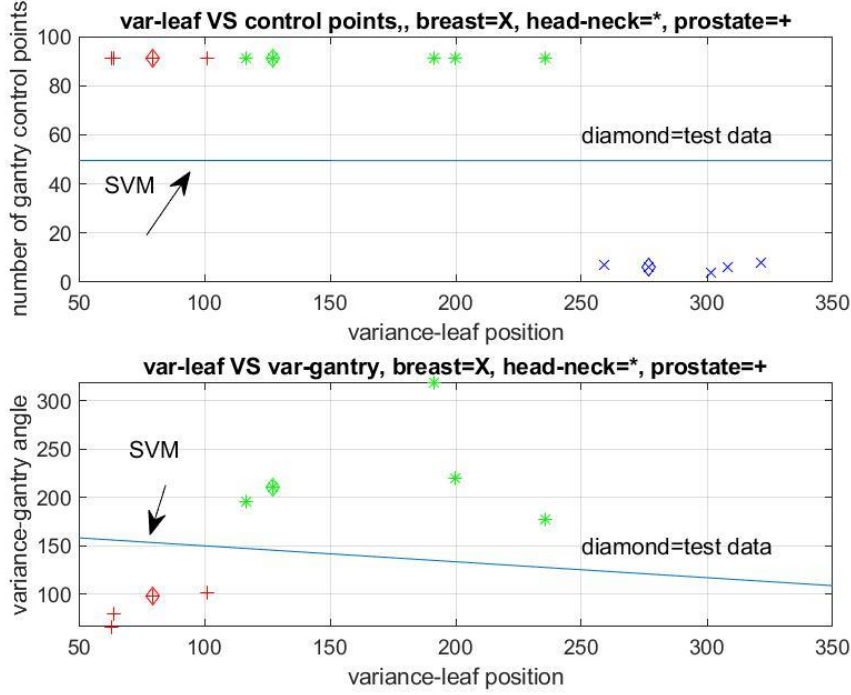


Figure 9. The bottom diagram is SVM applied to a 2-class problem, (head-neck and prostate) cancer treatments vs breast cancer treatments. The top diagram is SVM applied to a 2-class problem, head-neck cancer treatments vs prostate cancer treatments.

Tests are exactly the same as in the SVM case. The identified model of the testing treatment plan was calculated based on the training data only and no validation was known when the classification was carried out. Then, validation was tested on the three validation data: one head-neck, one breast and one prostate. A validation was successful if the 3-nearest neighbor constructed by the remaining 11 training sets can individually identify three validation data correctly. A validation was failed if any one of three validation data was misidentified. There were $5 \times 5 \times 4 = 100$ different combinations. In validation, all 100 tests were successful as in Table 2 for various w 's or we achieved a 100% success rate with a 0% failure rate. To illustrate, we show the most unfavourable and difficulty case for breast, prostate and head-neck cancer treatments respectively in Figures 10, 11 and 12 with $w=5$. Figure 10 shows the minimum ball that contains the validation point of prostate cancer treatments and additional three points. Obviously all 4 points belong to the prostate cancer treatments. Figure 11 shows the minimum ball that contains the validation point of head-neck cancer treatments and additional three points. Obviously all 4 points belong to the head-neck cancer treatments. Similarly, Figure 12 shows the minimum ball that contains the validation point of breast cancer treatments and additional three points. Obviously all 4 points belong to the breast cancer treatments. These three figures demonstrate why K-nearest neighbor method works for our problem.

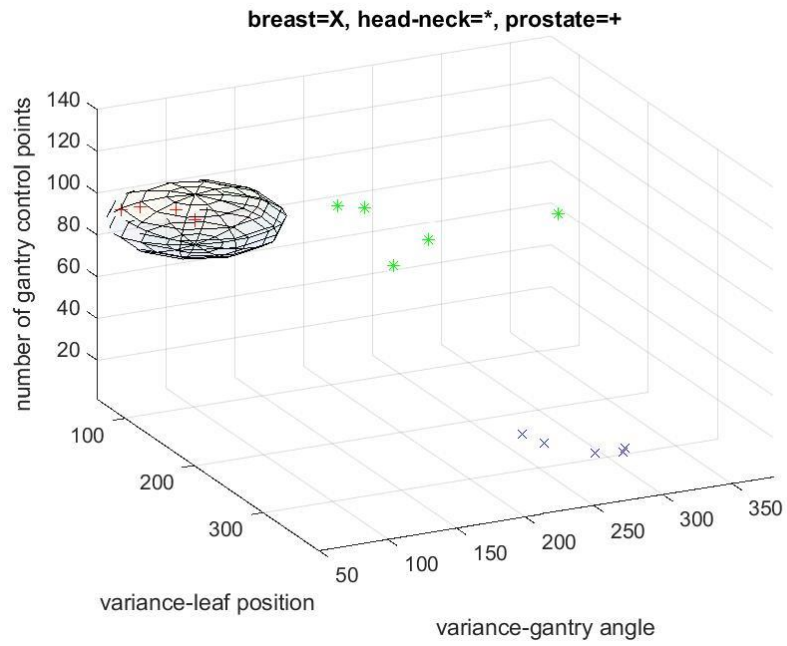


Figure 10. Illustration of K-nearest neighbor for prostate cancer treatments

Table 2. Successful and failure rates among 100 K-nearest neighbor tests for various w 's.

w	# of Tests	# of Success	# of Failure
1	100	100	0
2	100	100	0
3	100	100	0
5	100	100	0
10	100	100	0

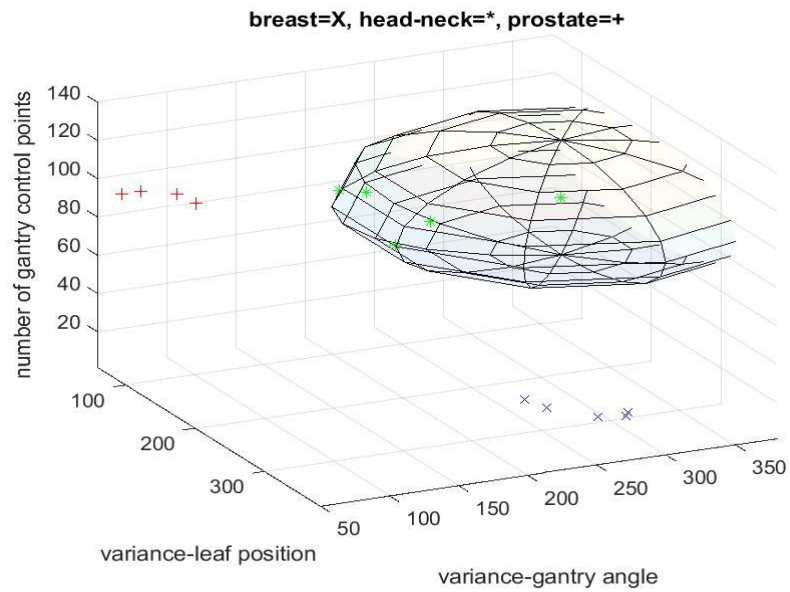


Figure 11. Illustration of K-nearest neighbor for head-neck cancer treatments

5. BAYES APPROACH AND THE LINEAR DISCRIMINANT ANALYSIS

The previous two algorithms are deterministic in nature and the algorithm to be developed in this section is based on some statistical models, specifically Gaussian distributions. Also in the previous two methods, no prior information is assumed and used. In real applications, however, prior information does exist that should be exploited and incorporated into algorithms. For instance, if a treatment plan is intended for head-neck cancer and is to be verified by the algorithm, the prior probability $p(hn)$ that the plan is for head-neck cancer is higher than the prior probabilities of $p(br)$ intended for breast cancer and $p(pr)$ intended for prostate cancer, where $p(hn)+p(br)+p(pr) = 1$ and $ps=prostate$, $hn=head-neck$, $br=breast$.

The idea of Bayes approach is to exploit this prior information. In the current study, there are three types of treatment plans $C = \{br, pr, hn\} = \{breast, prostate, head-neck\}$. Given a test vector or plan x , that is a 3-dimension vector representing the average of variation along the leaf number direction, the average of variation along the gantry angle direction and the number of the gantry control points, the goal is to find out which probability $p(C/x)$ is the largest for the given x . Precisely, we calculate all three possible probabilities

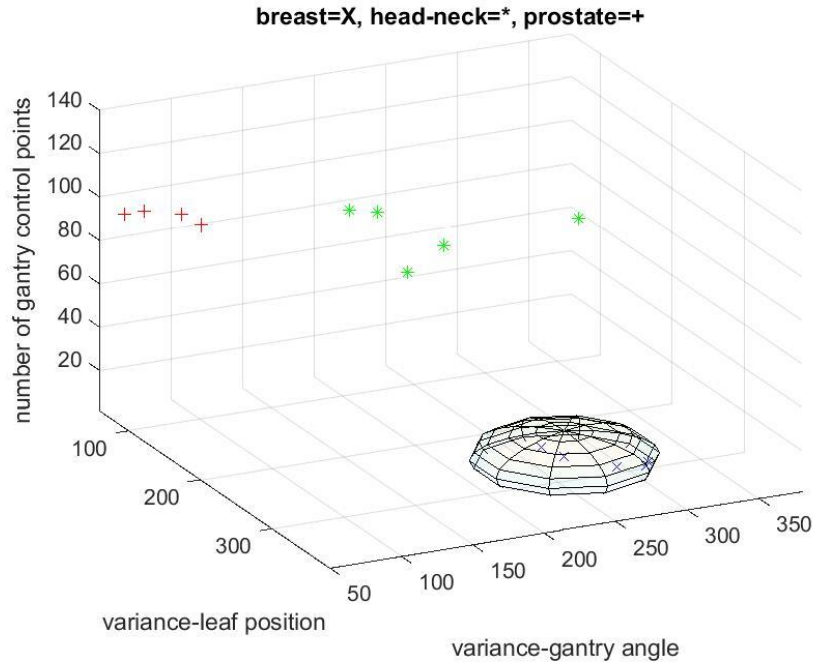


Figure 12. Illustration of K-nearest neighbor for breast cancer treatments

$$p(br|x), p(ps|x), p(hn|x)$$

the treatment plan label corresponding to the largest probability is the identified treatment plan. For instance, if

$$p(br|x) > p(ps|x), p(hn|x)$$

we say the treatment plan x is identified for the breast cancer by the algorithm. Now the question is how to compute. By Bayes theorem,

$$p(C|x) = \frac{p(x|C)p(C)}{p(x)}$$

Where $C = \{br, pr, hn\} = \{breast, prostate, head - neck\}$. Since $p(x)$ is the same, we only have to compare

$$p(x|br)p(br), p(x|ps)p(ps) \text{ and } p(x|hn)p(hn), \quad 5$$

Where $p(hn)$, $p(br)$ and $p(pr)$ are the prior probabilities. Again such information does exist. For instance if a treatment plan is intended for breast cancer and is up to check by the algorithm,

$$p(br|x) > p(ps|x) = p(hn|x)$$

Where $p(pr/x) = p(hn/x)$ is for simplicity assuming no other prior information is available. To calculate $p(x/C)$, we adopt the standard approach in the literature. First $p(x/C)$ is assumed to be Gaussian

$$p(x|C) = \frac{1}{|\Sigma_C|} \exp\{-(x - m_C)^T \Sigma_C^{-1} (x - m_C)/2\}$$

where the mean value and covariance matrix are computed by the training data in the class C . Second, logarithm is a monotone function and so we may compare

$$\log(p(x|C)p(C)) = -(x - m_C)^T \Sigma_C^{-1} (x - m_C)/2 - \log |\Sigma_C| + \log(p(C))$$

So (5) becomes

$$\operatorname{argmin}_{C=br,ps,hn} -(x - m_C)^T \Sigma_C^{-1} (x - m_C)/2 - \log |\Sigma_C| + \log(p(C))$$

This is referred to as the Quadratic Discriminant Analysis (QDA) in the literature [11]. QDA may be simplified by assuming that $\Sigma_a = \Sigma_{br} = \Sigma_{hn} = \Sigma_{ps}$, i.e., the variance is the same and calculate by all training data. This simplification results in the Linear Discriminant Analysis (LDA) in the literature [11]. Based on the LDA, the identified treatment plan is defined as

$$\begin{aligned} \text{treatment plan} = \operatorname{argmin}_{C=br,ps,hn} \{ & -(x - m_{br})^T \Sigma_a^{-1} \frac{(x - m_{br})}{2} + \log(p(br)) \\ & -(x - m_{ps})^T \Sigma_a^{-1} (x - m_{ps})/2 + \log(p(ps)) - (x - m_{hn})^T \Sigma_a^{-1} (x - m_{hn})/2 + \log(p(hn)) \}, \end{aligned}$$

6

Now the Bayes approach based on LDA can be summarized as follows:

1. Collect data.
2. Calculate the sampling average m_{br} based on breast training data only, the sampling average m_{hn} based on head-neck training data only and the sampling average m_{ps} based on prostate training data only. Further calculate the variance Σ_a by using all training data.
3. For each test treatment plan x , assign a prior probability $p(C) = a$ if the test plan is intended for the C cancer treatment and $p(nonC) = b = (1 - a)/2$ for other two non- C cases, where $1 > a > b > 0$ represents the prior knowledge that the plan was intended for C cancer. For instance, if the test plan x is intended for breast cancer, $a = p(br) > p(ps) =$

$p(hn) = b$, where $p(hn) + p(br) + p(ps) = 1, a + 2b = 1$ and $b = p(ps) = p(hn)$ is for simplicity alone.

4. Apply (6). The treatment plan label corresponding the largest value is the identified treatment plan.

To test the proposed algorithm, the same training and testing data as in the previous algorithms was used with various values of a and $b = (1 - a)/2$. The results are shown in Table 3. Again, we have achieved 100% success rate and 0% failure rate.

Table 3. Successful and failure rates for various a and b , Bayes+LDA

a	$b=(1-a)/2$	# of Success	# of Failure
0.36	0.32	100	0
0.5	0.25	100	0
0.7	0.15	100	0
0.9	0.05	100	0

6. CONCLUSION

Though very encouraging, the study was limited to three types of cancers, head-neck, breast and prostate cancers. To be useful, many more types of cancer treatment plans have to be collected, analyzed and tested. Followings the potential further research directions:

- The current study is based on a small data set. Nevertheless, it is promising and reassuring that Machine Learning algorithms can be effectively adopted in Automatic Radiation Treatment Plan Alert System. To make the study reliable, we plan to collect a large number of data. In addition, statistical analysis will be a part of study, especially error analysis.
- With more types of treatment plans and various complexity of different treatments, however algorithms becomes more involved. It is not guaranteed that linear SVM, K-nearest neighbor and Bayesian algorithms developed in the paper would work. Alternative classifiers need to be investigated, including Kernel SVM where the choice of kernels can be completely data driven. Or based on the prior knowledge.
- With more treatment plans, there is a possibility that two variations alone discussed in the paper may not be sufficient. What are the extra features needed to be extracted? This is the most critical step for the success. Note there are some features that have not been exploited in our algorithm, such as total dose and spatial dose distributions. By adding these additional information into the algorithms, performance of the algorithm is expected to be improved substantially.
- As expected, fingerprints selection is a key that has to be effective and simple. Once the right fingerprints are selected, a choice of which machine learning algorithm seems less important at least in this study. All three algorithms work fine with 100% success rate and 0% failure rate.

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Authors' Contribution

Erwei Bai: selection of fingerprints, algorithm development and tests, writing draft. **Junyi Xia:** Problem formulation and data collection.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.