OPTIMIZATION ALGORITHM OF A HIGH DOSE-RATE BRACHYTHERAPY TREATMENT PLAN FOR CERVICAL CANCER PATIENTS IN ZAMBIA

By

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A dissertation submitted in partial fulfillment of the requirements for the degree of Master of Science in physics

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AUTHOR'S DECLARATION

I hereby declare that the project work entitled "**OPTIMIZATION ALGORITHM FOR A HIGH DOSE RATE BRACHYTHERAPY TREATMENT PLAN FOR CERVICAL CANCER PATIENTS IN ZAMBIA**" submitted to The University of Zambia is a record of an original work done by me under the guidance of G. M. Chishimba, M. Mwalaba in Department of Physics and M. Kanduza at the Cancer Diseases Hospital respectively. The work of this project is submitted in partial fulfillment of the requirements for the award of the degree of Master of Science in Physics. The results embodied in this thesis have not been submitted to any other University or Institute for the award of any degree or diploma

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APPROVAL

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ABSTRACT

The increase in availability of diagnostic tools and increase in awareness of cancer disease, has enabled the diagnosis of new cancer cases that were not previouslycaptured in Zambia. Today, the Cancer Diseases Hospital (CDH) treats over 3,200 cancer patients annually, a number significantly higher than the initial projection of 1,200 when CDH was established. Approximately 60% of these patients require Radiotherapy (RT), and Brachytherapy (BT) is an essential component for treating cervical cancer. At CDH, BT treatment planning employs a computerized treatment planning system based on the report by Task Group 43 (TG-43) of American Association of Physicists in Medicine (AAPM) that generates radiation dose distributions for optimal treatment delivery. Although individualized plans can be developed from standard treatment plans, high patient volumes necessitate generating multiple standard plans tailored to suit most patient profiles. However, there is a need to verify the accuracy of these standard plans. This study aims at refining strategic decision points for passing or failing the standard treatment plan used at CDH by developing a mathematical modeling algorithm that evaluates current practices in optimizing. This is achieved by developing brachytherapy standard treatment plans. Using a retrospective study design spanning three years (2019-2021), we reviewed 254 treatment plans and collected data by reviewing source details from radioactive source parameters and dose-volume histogram markers to calculate various dose metrics necessary for quality assurance purposes. The study used some dose metrics to develop an algorithm capable of determining whether a given plan passes or fails based on quantitative evaluation criteria. While values for the Conformity Index (COIN), Conformity Number (CN), and Coverage Index (CI) were better in 2019 compared with other years; Dose Non-Uniformity Ratio (DNR) and Dose Homogeneity Index (DHI) remained low throughout all years reviewed. Nonetheless, most analyzed treatments had acceptable values for COIN, CI, and CN with mean values ranging between 0.86 (±0.09) to 0 .93 (±0 .05). Ideal case entails that these indices are of the value 1 or close to 1 except for DNR where a value of 0 is ideal. Unfortunately, none of the CDH standard plans examined passed the set criteria (i.e. 5 indices passing out of the 5) because none of them met standards for both DNR and DHI indices whose average values ranged between 0.34 to 0.43 for DHI and 0.57 to 0.66 for DNR. Therefore, achieving treatment plans that meet optimum balance among these indices require that organs at risk are not exposed beyond their tolerance limit but, providing maximum coverage of clinical target volume should be considered. This Algorithm will serve as an institutional protocol devised for acceptability criteria of a treatment plan at CDH.

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LIST OF ABBREVIATIONS

AAPM – America Association of Physicists in Medicine

BT – Brachytherapy

CDH – Cancer Diseases Hospital

CI – Coverage Index

CIMP - Comité International des Poids et Mésures

CN – Conformity number

COIN – Conformity Index

CTV – Clinical Target Volume

DHI – Dose Homogeneity Index

DNR – Dose Non-Uniformity Ratio

DVH – Dose Volume Histogram

GEC – ESTRO - Groupe Européen de Curiethérapie (GEC) and European Society for Radiation And Oncology

HDR – High Dose Rate

LDR – Low dose rate

OAR – Organs at Risk

PD – Prescribed Dose

QA – Quality Assurance

QC – Quality Check Radiotherapy & Oncology.

RT - Radiotherapy

TG-43 – Task Group 43

TPS – Treatment Planning System

UTH – University Teaching Hospital

CHAPTER 1

1. INTRODUCTION

1.1 Background

Cancer is among the leading causes of death in the world, particularly the older populations, are the most affected. According to the Global Burden of Diseases 2015 study (GBD 2015) [1], after cardiovascular disease, cancer ranks as the second most common cause of death worldwide. Cancer treatment is challenging mainly because one has to successfully irradiate the tumor while sparing the healthy tissues and Organs at Risk (OAR) [3]. Hence the need for constant optimization of the treatment plans. Advanced techniques also require stringent optimization methods to improve treatment delivery and achieve favorable outcomes.

Cancer may be treated using a number of ways, for example by radiation, chemotherapy, and surgery. These methods of cancer treatment can be used individually and/or in some cases can be combined depending on the disease stage and type of cancer, to achieve positive outcomes, Mayo Clinic [4][5]. Radiation therapy is the common treatment modality used in treating carcinoma of the cervix at CDH. Radiation therapy aims to destroy the tumor as much as possible while causing the least amount of damage to the surrounding healthy tissue. To do this, a radiation beam is pointed in multiple directions toward the tumor to deliver the highest dose there, Cameroon [7]. In brachytherapy (BT), the malignant cells are destroyed by putting a radiation source inside or next to the tumor, Anderson [8]. This radiation can either be delivered externally at a distance (i.e. Tele therapy) or at a short distance (i.e. Brachytherapy). Brachytherapy is categorized into two groups; high dose rate brachytherapy (HDR) and low dose rate brachytherapy (LDR). A low Dose Rate involves placing radioactive seeds permanently or temporarily in the tumor (e.g. prostate) to deliver radiation over an extended period of time while a High Dose Rate involves placing flexible needles into the tumor to deliver a very high dose of radiation over a period of few minutes. This study, however, will focus more on HDR brachytherapy which is the most frequently used method in treating carcinoma of cervix. Two forms of high-dose-rate brachytherapy treatments exist, intracavitary brachytherapy, in which catheters are inserted into the body cavity, such as the uterus or cervical region, and interstitial brachytherapy, in which catheters are inserted into the tumor

tissue, such as the prostate tumor [2]. The benefit is that the tumor receives a very high dosage while the surrounding normal tissues receive very little radiation. Banerjee [3]. Due to its harmfulness, three factors are taken into consideration when determining how much radiation is to be used, that is: the type of radiation, the type of cell, and the environment. Additionally, high-dose brachytherapy (HDR) needs to be optimized because of the short treatment times (i.e. average time of 10 min)which limit time for correcting errors, and this may increase the risk of excess dose to nearby healthy tissues and organs of the patients in case of errors. It follows that the use of BT treatment requires accurate and precise dose calculations to minimize radiation to healthy tissues. Computer-based treatment planning is used in the process of optimization using customized computer algorithms.

The success of the entire process depends on how well a treatment plan is carried out. Optimization is a crucial phase in the radiation therapy treatment planning process. Today, treatment planning for HDR brachytherapy routinely includes mathematical modeling and optimization, Morén [9].

Uncertainties in dose calculations exist and knowledge of these uncertainties provides a benchmark for the quality of a treatment plan delivery. Several factors bring about these uncertainties, some of them being, patient morphology, the location of the tumor, source movement (due patient movement), and patient radio-sensitivity etc. It is also important at this point to note that it is not fairly easy to account for all possible influences when it comes to uncertainty determination.

At the Cancer Diseases Hospital (CDH), the HDR brachytherapy process involves both pre- and real-time treatment planning. The processes have a distinct workflow which includes optimization by fine-tuning the treatment plan for effective delivery of the desired dose. The pre-treatment plan is created based on a standard plan. Standard plans are general plans created and used to treat several patients with similar profiles while an individualized plan is one that has been tailored to suit that particular patients based on the Computer Tomography (CT) images. The creation of the plan is based on clinical findings at the time of treatment and can be individualized to the patient. Real-time planning is based on creating a plan while the patient waits, and this can be a lengthy process. The workflow for the two planning options differs at the point of treatment planning where

the real-time planning requires a decision to be made based on diagnosis by the radiation oncologists and medical physicists.

The Cancer Diseases Hospital uses the International Commission on Radiation Units and measurements (ICRU) report for dose reporting. Dose reporting simply means providing information on how patients were treated by reporting the dose that was given to a particular volume. However, this study tries to bring in an extra way of reporting doses by using dose indices. The study aimed at verifying if what is being reported using ICRU report can be assessed through another parameter as a second check, through a mechanism that can refine and have strategic decision points for passing or failing the standard BT treatment plans being used in treatment delivery.

1.2 Statement of the Problem

The diagnosis of new cancer cases in Zambia has been on the rise thanks to the advent of improved diagnostic tools and awareness campaigns to the public. The CDH attends to about 3,200 cancer patients per year that is over 2000 patients above the 1,200 projected when the CDH was established. About 60% of the patients require Radiotherapy (RT), Kanduza [10]. Brachytherapy is a component of RT and is a gold standard for the treatment of cancer of the cervix. At the CDH, treatment planning for BT is done using a computer-based algorithm that generates radiation dose distributions for treatment delivery. The treatment plan is standardized, and an individualized plan can be drawn from the standard treatment plan. High patient loads necessitate the generation of several standard plans that suit the majority of patient profiles. However, no confirmation has been done to ascertain if the standard plans adequately deliver the correct dose.

1.3 Aim of the Study

To develop an optimization algorithm that would ascertain the dose delivered in a standard BT treatment plan is adequate for a high-dose-rate brachytherapy procedure by calculating dose metrics.

1.4 Research Objectives

The following were the objectives of this study:

i. To calculate brachytherapy dose metrics applied in treatment plan quality assurance.
ii. To develop an algorithm to determine whether the standard treatment plans being used deliver acceptable doses.

1.5 Research Questions

i. How are the dose metrics of the treatment plans calculated?
ii. How does the algorithm improve/affect the efficiency of a standard BT treatment Plan?

1.6 Significance of Study

A study done by Jayakody [12], reviewed the need to verify the optimum dose calculated by TPS using an independent testing method in order to eliminate under/over irradiation of the tumor region. This is done as part of Quality Assurance (QA) routinely. At the CDH, however, this does not seem to be the case. This study will provide means of easy routine to verification of dose adequacy and/or adopted methods for cancer treatment being used. The results of the study may be used to streamline the treatment planning process and aid in decision making thereby improving the efficacy of the standard treatment plan. Additionally, the results will help improve the efficacy of the treatment planning process, and hence cut down on the treatment planning time.

1.7 Limitations of the Study

The major limitation of this study is the fact that it is purely computational physics, this means that it has no clinical correlation. The patient's files were not checked for information on disease staging and other factors that could have had direct impact on the results of the calculated dosimetric indices.

The second challenge faced was finding the recommended thresholds for some of the dose indices. Very few studies have been done on what dosimetric threshold to accept for a good cervical implant. However, majority of the studies done showed average values of the various indices. For the purpose of this study, mean dose indices that were close to ideal values of 1 and 0 where adopted. This, however, can impact on some of the indices failing thus leading to biased results. The study is a dosimetric analysis, not an overall survival of the patients.

1.8 Structure of the dissertation

The dissertation has five chapters in total of which the first chapter is an introduction and summary of the whole dissertation. It contains the statement of the problem, aim, objectives, and the significance of the study. A review of literature relevant to the study is presented in the second chapter while the methods and materials are presented in the third chapter. Chapter four presents the data analysis and the results of the study while chapter five highlights the findings and discussion of results and lastly, chapter six gives the conclusion and the recommendations for future work.

CHAPTER 2

2. LITERATURE REVIEW

2.1 Introduction

Minimizing complications to normal tissue is the goal that drives all cancer treatment plans. Therefore, many components of the workflow for cancer treatment planning may involve optimization problems, thereby opening the door to the creation of mathematically sound treatment planning techniques, Maas [11]. The purpose of this review is to give an overview of some of the optimization models being developed and used to provide an understanding of the expected outcomes.

2.2 Dose verification

Jayakody [12] explains how to check the dosage when receiving HDR brachytherapy for cancer. Before administering the actual treatment, the Treatment Planning Systems (TPS), which are managed by computer algorithms, are crucial in determining the ideal dosages for the tumor region and the organs that are in danger. As part of quality assurance (QA), the determined optimal dose by TPS must be confirmed using a testing technique to rule out under or over-irradiation of the tumor location. Research has indicated that there exist two distinct categories of independent dosage verification techniques: computational and experimental. They are employed to verify the dosages determined by TPS. Jayakody [12] did a review and summary of the studies done in the past 10 years on the BT treatment planning verification and, they analyzed the reliability and limitations. The study's findings demonstrate that verifying the dose distribution during BT treatment using a technique helps in ascertaining the patients' dose and improving the treatment plan. Furthermore, the outcomes indicate that it offers the chance for QA and quality check QC of the BT treatment. Jayakody [12] further noted that improvements are required in dose verification methods to cater to the rapid developments in clinical and scientific techniques related to BT treatment.

Gabriel et al. [13], in Physics and radiation oncology journal indicated that therapy delivery verification is not always available, which might sometimes result in systematic errors that lie undiscovered for a very long time. On the other hand, new research indicates that greater focus is

being placed on making sure that BT treatment is properly monitored and/or verified. Further, Zaorsky [14] has brought to light the fact that, with the introduction of image-guided brachytherapy and comprehensive treatments that involve patient-specific optimization in order to give a very high dosage of up to 15 Gy in a single fraction, the requirement to precisely validate the dose distribution computed by the TPS has increased significantly.

Kumar [15] did a study on the dose verification method for HDR brachytherapy treatment plans. The study aimed to evolve a fast dose verification method for a high dose rate BT treatment plan and to try and demonstrate its applicability in different clinical cases. They used a software tool in VC++ programming language on a Varisource HDR unit (afterloader) for high dose rate dosimetry plan verification using TG-43 parameters. The report by TG-43 of AAPM has been known as the most common formalism for obtaining dose distribution around brachytherapy sources and the treatment planning systems. The study's findings demonstrated that, for the majority of the dosage points computed. There was a 3% agreement between the TPS-derived dose levels and the verification code-calculated values. Using TG-43 values, they were able to confirm a quick and independent technique of dosimetry verification at certain locations in the HDR brachytherapy treatment plan through clinical cases. The code that was created could function with Varisource. Further, Kumar [15] observed that by utilizing the fitting constant of the appropriate radioactive source, it might be altered for different radioactive sources. The reviews conducted thus far show that therapy efficacy can be guaranteed using independent dose verification methodologies. The Algorithm developed in the current study will act as an independent way to verify dose adequacy during the treatment planning process.

2.3 Sources of Uncertainty

In brachytherapy, a high dose is used to treat cancer, and this is done whilst ensuring that the organs at risk are being spared. Gabriel et al., [13] demonstrated further that the steep dosage gradient attribute, defined as the difference between the effective radii of spheres equal to half and full medical prescription volumes, is responsible for producing the intended consequences (i.e it can irradiate a large dose to the tumor while reducing the OAR dose easily. Additionally, it is noteworthy that the dose gradient becomes steeper with decreasing distance (i.e from source to CTV). Although this seems to be a good thing, there are still some ambiguities and errors occurring

in the process. Besides the treatment procedure relies on several manual stages that may be susceptible to errors.

The following treatment planning aspects of brachytherapy; imaging, dosage delivery, target volume, applicator displacement, anatomic vibrations (motions) and source strength, are not without uncertainty. For additional clarification on a few of them, source strength has demonstrated that source strength for photon-emitting devices can be specified uniformly in brachytherapy in terms of air-kerma strength (i.e. the product of the calibration distance squared and the air kerma rate at that distance), Kiristis [18]. A report by De Leeuw [20] highlights the main sources of uncertainty in BT for cervical cancer as being; source calibration, dose, and dose-volume-histogram (DVH) calculations; additionally, applicator reconstruction, contouring, intra-faction and inter-fraction uncertainties, and dose delivery are all involved. The current method of BT dose calculation formalism being used in treatment planning is based on the AAPM Task Group-43 (TG-43). Jo [21] observed that, particularly during inter-fraction treatments, application displacement happened at random. Within the dose distribution, applicator displacement-related uncertainty in dose administration is quite relevant. Another source of systematic uncertainty is the placement mistake of the treatment needles inside the implants. The patient's consistency as well as the device's (sources') geometry during treatment planning and delivery affect positional precision and dosage delivery accuracy. The applicator type, design, source orientation, and clinical target volume are the variables that will affect the uncertainty. While the orientation of curved applicators can be variable and not tangential to the source route, the orientation of straight applicators is roughly aligned to the source path axis. Applicator displacement uncertainties may include the omission of dwell positions and the shifting of all dwell positions by a predetermined amount of distance.

Determining the accuracy of measurements and computations by quantitative means requires an understanding of uncertainty. The Comité International des Poids et Mésures (CIMP) report by Kirisits serves as the foundation for uncertainty definitions and the present standardized approach for analyzing and communicating measurement uncertainties [18]. It is also important to note that this method categorizes uncertainties into either type A (those evaluated by statistical methods) or type B (those evaluated by other means). The dose indices calculated will provide a quick way of

knowing where the error could have come from as they are homogeneity and conformity indicators.

2.4 Management of uncertainties

A number of measurements are made at different distances between the radiation source and the ionization chamber in order to remove uncertainties that arise from the afterloading system's positioning of the source (roughly 0.3 mm). A calculation is done to determine the source's positioning. Type A (statistical) and type B (everything else) uncertainties are the two categories of uncertainties that were previously mentioned Dewerd [17]. Type A uncertainties which are a result of systematic effects of after-loader accuracy can be verified at commissioning and during precision checks. Kirisits [18] observes that although systematic movements caused solely by the after-loader may be calibrated and eliminated, the accuracy of source location during treatment is still pending. By appropriately localizing and defining the source path during commissioning and/or treatment planning, type B uncertainties can be significantly reduced, Hellebust [22]. It is important to note that, there is a possibility to minimize many of these uncertainties by digitizing the real source path during applicator commissioning and using this path for treatment planning.

2.5 Dose Optimization of HDR brachytherapy treatment plan

In circumstances where treatment planning is done manually, the planning takes a long time as trial-and-error techniques are used. In reality manual treatment requires special skills and experience, while optimization can reduce over reliance on human involvement, Morén [9]. This is where the use of optimization models comes into play as it has the potential of saving time and improving treatment plan quality. This is evident in the following studies [22, 23]. Optimization models and algorithms are being developed also because of the limited amount of computing time available for treatment planning process and at the same time help in achieving the optimal dose distribution, especially optimization algorithms for HDR [9]. Manual planning is a laborious procedure that requires numerous simulations. Therefore, automated techniques are being developed to rectify inconsistencies resulting from the first manual process. Oud et. al [23], have also shown in their work that optimization and use of algorithms resulted in clinically favorable plans and auto-planning took an average of 20.5 seconds compared to 15 -30 min for manual planning.

A study was done by Sharma [16] on dose optimization in gynecological 3D image-based brachytherapy by employing the Martinez universal perineal interstitial template (MUPIT) where a plan evaluation was

done by compiling dosimetric outcomes qualitatively and quantitatively using cumulative dose histogram for various dose indices and GEC-ESTRO DVH parameters (i.e. the volumes of the CTV & OARs getting prescribed dose). The following indices were considered in this study; coverage index (CI), dose homogeneity index (DHI), overdose volume index (OI), dose non-uniformity ratio (DNR), external volume index (EI), and conformity index (COIN). Results from this study show that the evaluated mean values for the indices were as follows; CI of 0.86 ± 0.03 with a range of 0.79 – 0.92. The mean value for DHI was found to be 0.69 ± 0.11 with a range of 0.51 – 0.87. The mean value for DNR was found to be 0.31 ± 0.09 with a range of 0.11 – 0.43. The mean for COIN was 0.79 ± 0.05 with a range of 0.71 -0.85, Sharma [16]. In the same study, they further highlight the usefulness of dose-volume indices and dose-volume parameters of the CTV and OAR during interstitial gynecological brachytherapy. These parameters help maintain the uniformity of optimization among the users to yield more accurate information regarding normal tissue tolerance and establishment of a dose-response relationship in the future.

It is important to note that the conditions for an ideal implant are; CI = 1, DHI = 1, DNR = 0, COIN = 1 and CN = 1, Kehwar[19].

2.6 The use of machine learning in the optimization of HDR brachytherapy

Machine learning is simply a form of statistical inference that uses known properties of training data to predict novel solutions to problems. It also can accumulate new knowledge during training and apply it to future cases. Most of the optimization techniques available can solve the optimization problem with the given weights (e.g. dwell times, isodose line etc.). In the past, these weights were adjusted manually to yield a high-quality plan and this task is labor-intensive, time-consuming, and generally affects the final quality of the plan. Machine learning, however, brings an automated weight-tuning approach to adjust the weights. Shen et al [24] developed a weight-tuning policy network for inverse treatment planning in high-dose-rate brachytherapy that improved the timing.

Some of the articles reviewed show similar work where several systems and techniques have been developed and are being used to verify dose delivery. Palmer et al [25] highlight some of these techniques that have been developed for example, the Fiber Optic Dosimetry System (FODS) developed by Suchowerska et al, which measured urethral and rectal wall doses in the HDR

prostate patients. The study shows knowledge of the actual dose delivered could be used to give a warning of potential over or under-dose. Similar to this, is the use of detectors to check dose delivery for example the Metal Oxide Semiconductor Field Effect Transistor (MOSFET) detectors for in vivo dosimetry.

From the literature reviewed so far, it is evident that several optimization models and techniques are being used and more are yet to be developed as this subject is an active field of research. For example, the penalty model, whose purpose is to penalize doses being higher or lower than specified values (i.e., it gives a penalty if the doses are outside specified intervals). Dalwadi [27]. In a similar manner, machine learning is being widely employed, particularly in the vital sectors of radiation and medicine. Additional reference can be made to Wang [28] for his evaluation on machine learning methods that are applied to radiotherapy. The introduction of computer optimization algorithms in cervical cancer treatment planning has demonstrated tremendous improvements. The algorithm developed in this study is another computer optimization algorithm that seeks to improve the current planning system by adding a verification stage before a treatment is administered.

CHAPTER 3

3. RESEARCH METHODOLOGY

3.1 Introduction

This chapter provides the research methods used to undertake this research. The chapter has four sections. The first section outlines the type of research design used. Section two provides the sampling frame while the third section provides the sample size and sampling technique used. The fourth section outlines the data collection techniques.

3.2 Research design

This research used a retrospective study approach. In this type of study, the data is collected from the records, implying that the outcomes have occurred in the past. Wang and Kattan [29] gave a detailed explanation of cohort studies (i.e., the design, analysis, and reporting). They described a retrospective study as one which is done after subjects have already developed the outcome. The investigators go back in time to identify a cohort of subjects at a time when they did not have the outcome. Vandenbroucke [30] noted that even though the prospective cohort study design where individuals are followed over time and data is collected as their characteristics or circumstances change, is ranked higher in the hierarchy of evidence than a retrospective design. The information gained from a retrospective study can help plan a future prospective study. Additionally, it essentially has all the benefits of a cohort study.

3.3 Sampling frame

The sampling frame was the Cancer Diseases Hospital (CDH) at the University Teaching Hospital (UTH) in Lusaka, Zambia. The treatment plans that were reviewed are for cervical cancer patients from 2019 to 2021.

3.4 Sample size and sampling technique

Census sampling was used where all the treatment plans for patients from 2019 to 2021 (i.e., 189 patients) in total were reviewed. Due to missing parameters or data and incomplete plans, the total number dropped to 145 patients. In 2019, 51 patients were treated while 38 patients were seen in 2020 and 56 in 2021.

3.5 Data Collection Techniques

The study reviewed 254 treatment plans of the 145 patients who were treated for carcinoma of the cervix using Iridium-192 and different applicators. Applicators vary depending on the patient's disease and anatomy. Majority of patients were treated using applicators with only two catheters while others were treated with those having 3 or more catheters. Data was collected from the Ocentra Brachytherapy treatment planning system used at CDH. These plans were created according to the clinical protocol (TG 34) formalism. Data was collected by reviewing source details and the following dose volume histogram markers were collected to enable the calculations of various dose metrics; dose in cubic centimeters [ccm], the volume at 100% of prescribed dose (V_{100}), Volume at 150% of the prescribed dose (V_150), Patient Target Volume (V_{PTV}), Dose reference Volume (V_{Dref}), Planning Target Volume (PTV), Clinical Target Volume High Risk (CTV_{HR}), number of Organs At Risk (OAR), Volume of the critical structure covered by the prescription isodose (V_{OARref}, i), Volume of the OAR (V_{OAR}), Patient Target Volume at 100% but expressed as a volume (PTV_{ref}), Total volume (Tot_{ref}), The doses at point A (applicator points) both absolute and real dose. Calculations were done to determine the dose indices.

3.6.0 Data Analysis

3.6.1 Introduction

This section highlights the process undertaken to analyze the data. The first section highlights how the extracted data was cleaned followed by the various formulas used to calculate the respective dose metrices, and lastly the software used to write the algorithm.

3.6.2 Data Cleaning

The extracted data was cleaned by discarding treatment plans that were incomplete or had missing parameters. The initial sample size had a total number of 189 patients, of which 18 treatment plans were not in the Treatment Planning System (TPS), hence the total sample size was reduced to 153. Secondly, we had 26 patients whose treatment plans had unspecified volumes for some of the OARs, the majority coming from 2019, thereby bringing the total sample size to 145 treatment plans.

3.6.3 Dose Metrics

In order to evaluate the quality of the BT strategy, GEC-ESTRO has established metrics and indices such as conformity indices and homogeneity indices [32]. Regardless of the optimization technique, the indicators support the objective evaluation of the treatment plan and aid in the detection of hot and cold regions, as well as assertion for the target coverage, and limit the dose to the OAR, Poddar et al. [32]. This study uses a selected number of these indices; conformity index (COIN), coverage index (CI), conformity number (CN), dose homogeneity index (DHI), and dose non-uniformity ratio (DNR) to assess the quality of plans being used at CDH. Optimal values of these indices can be used in dose optimization as they yield higher coverage of the clinical target volume (CTV).

Conformity Number (CN) is a measure of conformity. In addition to accounting for the dose to the PTV, it also takes into account the proportions of the OAR that receive higher than the prescribed dose. The formula for conformity number is given by Morén [9] as:

$$CN = V_{100}^{PTV} x \frac{PTV_{ref}}{Tot_{ref}}, \qquad 1$$

Where PTV_{ref} corresponds to V_{100}^{PTV} but is expressed as a volume, and Tot_{ref} is the total volume (with both PTV and OAR included) which receives at least the prescription dose.

CN takes the value between 0-1, with 1 being the best possible value in the measure. A value close to 0 indicates either a total absence of conformity which means that the target volume is not irradiated, or a very large volume of irradiation compared to the target volume Morén [9]. For this study, a value of 0.65 will be adopted because it's the highest average value from all studies reviewed and secondly, it's close to 1 which is the ideal value, see Reference [33].

Conformal Index (COIN) is a measure of how well the distribution of radiation conforms to the shape of the radio surgical target. The COIN used in this study is that which takes into account the critical organs. Baltas et al. [34] used the Conformity Number (CN) by adding a supplementary parameter, organs at risk (OAR), Baltas [34]. This index was defined as follows:

$$[COIN = CN\ x\ \prod_{i=1}^{N_{OAR}}(1 - \left(\frac{V_{OARref,i}}{V_{OAR,i}}\right))], \qquad 2$$

Where; N_{OAR} is the number of organs at risk, $V_{OARref,i}$ is the volume of the organ at risk covered by the prescription isodose and $V_{OAR,i}$ is the volume of the organ at risk. A COIN equal to 1 corresponds to ideal conformation, whereas if the COIN is greater than 1 it indicates that the irradiated volume is greater than the target volume and includes healthy tissues, and if the COIN is less than 1, the target volume is only partially irradiated. Since a value of unity is rarely achieved, any value close to 1 is said to comply. For example a COIN value of 0.8 implies unacceptable conformity in general.

Dose Non-uniformity Ratio (DNR) is simply the ratio of the volume encompassed by high but clinically tolerable doses to the volume that is covered by the reference isodose [35]. According to Strnad [35], the DNR is given by :

$$DNR = \frac{V_{150}}{V_{100}} \qquad 3$$

Where, V_{100} is the reference dose volume that receives a dose equal to or greater than the Prescribed Dose (PD), while V_{150} high dose volume is the volume that receives 1.5 times the PD or more. The optimal dose distribution in terms of dose uniformity can be achieved at the minimum DNR value. The Dose Non-Uniformity Ratio provides is an easy way to interpret parameters for quantitative analysis of dose homogeneity in interstitial implants Major [36].

The Dose Homogeneity Index (DHI), also called the relative Homogeneity Index (HI), has a similar concept to that of the DNR. Major [36] highlights the fact that there exist different definitions of DHI. However, the formula used in this study is from the practical handbook by Strnad [35], which is stated as

$$DHI = \frac{V_{100} - V_{150}}{V_{100}} \ \ or\ DHI = 1 - DNR, \qquad 4$$

Where, $V_{100}$and V_{150} are the relative volume of the Planning Target Volume (PTV) expressed as a percent of the clinical target volume irradiated by at least 100% and 150% of the PD, respectively.

Low values of DHI such as < 80% means that the implant is of poor quality. This is so because ranges outside the implanted region will be encompassed by the minimum dose and the absolute dose values of the high-dose areas will increase within the implant [35].

The Coverage Index (CI) indicates the proportion of the target volume that receives at least the reference dose. It represents a measure of the quality of target volume captured and it should be maximized. The limit is towards 1 [35]. It is the ratio of the volume of Clinical Target Volume High Risk (CTV_{HR}) receiving 100% of the prescribed dose to the total volume of CTV_{HR}.

The formula used was extracted from the practical handbook [35]:

$$CI = \frac{V_{PTV}(D_{ref})}{V_{PTV}} = V_{100} \ \text{ or } \ \frac{PTV_{ref}}{CTV_{HR}}, \qquad 5$$

Where V_{100} is the relative volume of the planning target volume (PTV) as a percent of the clinical target volume that is irradiated by at least 100% of the prescribed dose. PTV_{ref} is the reference planning target volume while CTV_{HR} is the high risk clinical target volume.

The ideal values of DHI, CI, COIN, and CN should be 1, and the value of DNR should be 0, Kumar [31].

3.7 The Algorithm

The algorithm was developed using the Python programming language software, see appendix p.67. Five dose indices were picked for this study and the calculation of these indices was performed within the algorithm. The following dose indices COIN, CI, CN, DHI, and DNR were used in developing the algorithm, and selected passing thresholds for individual indices were set. The program first imports the collected data into panda's dataframe and then calculation of the dose indices takes place. Recommended threshold values for acceptable cervical implant for each of these indices was used to then check if the indices were passing or failing. The next step is the evaluation of the plan were the outputs of each index are added together to check how many index passed. The plan was then evaluated and a check was carried out to see if it passed the set criteria of 5 indices passing out of the 5. The algorithm was developed to pass or fail a treatment plan using the calculated dose indices. Poddar [32] suggests that institutional protocols should be worked out in order for the acceptability criteria of the treatment plans to have uniform optimization across users in the institution.

For this particular algorithm, reference thresholds for the acceptability of each dose metric index were made for each acceptable cervical implant. Reference of these threshold has been made, majority of adopted threshold values are average values obtained from similar studies. They have been adopted as they were close to ideal conformity of value 1. Few of the thresholds adopted have been recommend as acceptable for a good cervical implant.

According to Sarkar [37], Python is an interpreted, interactive, object-oriented, and multi-purpose programming language created by Guido Van Rossum in the late 1980s. In a study conducted by Srinath [38], interesting features of Python programming language which makes it the fastest-growing programming language were highlighted. It is open-source language hence it can be used

to write a wide range of programs today. The fact that it has a graphical user interface (GUI), is among the reasons it was chosen over other programming languages in the current project.

For Conformity Index, the treatment it is said to comply with protocol if the 90% isodose covers all the clinical target volume. If 80% of the isodose covers all of the clinical and pathological target volume, the protocol violation is considered to be minor but if 80% of isodose does not cover all of the clinical and pathological target volume then the protocol violation is considered to be a major one [39]. For this study a threshold of 0.80 for COIN was adopted from a study done by Poddar [32]. He suggests that this value should be as high as possible while keeping the value of DHI into account.

Major et al. [39] suggested a CI of 0.95 for interstitial cervical implants. A study by Poddar et al. [32] showed that if attempts are made to further increase the CI, it increases at the cost of DHI, thereby increasing DNR, hence there is a need to strike a balance among the indices for a better optimal balance of all the parameters. In this study, a CI of 0.90 was considered as 90% of the target volume gets the prescribed dose which is not a major violation.

A conformity number (CN) is also said to comply when a value of 1 is achieved but since this is practically impossible. Taking into consideration that CN has a similar concept with COIN, 65% (CN >= 0.65) coverage of isodose on the clinical and pathological target volume was used in assessing whether CN complied with the protocol or not, Sharma et. al [33]. The value was adopted based on the fact that it was the highest mean value obtained from studies that calculated dose indices as there was no study categorically saying what threshold value to accept for CN for a good cervical implant.

The ideal dose homogeneity index (DHI) value should be 1, but it is practically impossible as the dose levels around the needles are very high. A threshold value of 0.50 for DHI was adopted from [45] for this study. According Podder et. al [32] this value was the mean value set as a threshold for their optimal plans (i.e., while using graphical optimization), reference to this can be made from Podder et. al [32]

Lastly, the dose non-uniformity ratio (DNR) has a similar concept to DHI except the ideal value for DNR is 0. Like the other cases, it is practically impossible to attain an ideal value of 0 but anything close to 0 can be accepted. For this study a value less than or equal to 0.30 was used as a threshold. In most cases the same threshold is used for breast implant acceptability, Strnad [22].

3.8 Statistical Analysis

The calculated parameters of the OARs and target were statistically examined using Python for Windows, version 3.11.4 64-bit. The least squares fitting was used and the slopes of the curves were obtained. The relationship between the dose indices was established.

3.9 Summary

The chapter highlights the research methods used, using a retrospective study approach. The target population was the female cervical cancer patients at Cancer Diseases Hospital at the University Teaching Hospitals in Lusaka, Zambia. The sample size comprised fifty-one (51) patients in 2019, thirty-eight (38) patients in 2020, and fifty-six (56) patients in 2021. No sampling was done because the population was too small. It also highlights the methods used to analyze the collected data. The various formulas used to calculate the dose indices are well explained with their significance.

CHAPTER 4

4.0 RESULTS

4.1 Introduction

This chapter shows the results of the calculated dose indices on key parameters used in Quality Assurance to get a quantitative evaluation. The calculated indices were then used to develop an algorithm using Python programming language. The order of presentation of the analysis is as follows: Results of the five dose indices, the block diagram of the algorithm used, and the output results from the algorithm.

4.2 Results of the calculated Dose indices and the Algorithm

Table 1: Participant's Demographics Table

	2 Catheters		More than 2 Catheters	
Year	**No. of treatment plans**	**No. Expressed as a %**	**No. of treatment plans**	**No. Expressed as a %**
2019	38	14.96	13	5.12
2020	23	9.06	37	14.57
2021	114	44.88	29	11.42

Table 1 shows the participant's demographics to understand the population for each group. Where a total of 51 treatments plans were reviewed in the year 2019 from which 38 plans had patients treated with applicators with 2 catheters, while 13 were treated with an applicator with more than 2 catheters. Similarly, 23 of the 60 treatment plans for 2020 were for patients who were treated with an applicator with 2 catheters and 37 with applicators with more than 2 catheters. A total of 143 treatment plans were reviewed for the year 2021 and 114 of these treatment plans were for the patients treated with an applicator with only 2 catheters and 29 with an applicator with more than

2 catheter. From the table we see the year 2021 had the highest number of patients compared to the other two years.

Table 2 shows the dose indices for the 2019 patients who were treated using an applicator with two catheters (Ring and Tandem).

Table 2: Calculated dose indices for 2019 patients treated with an applicator with two Catheters

TREATMENT PLAN	APPLICATOR TYPE/DOSE	No.of FRACTIONS	DHI	CN	COIN	CI	DNR
TP1	R34IU6_60_7Gy	1	0.350	0.810	0.810	0.900	0.650
TP2	R26IU4_60_7Gy	1	0.235	0.954	0.954	0.977	0.765
TP3	R34IU6_60_7Gy	1	0.434	0.845	0.843	0.919	0.566
TP3	R34IU6_60_7Gy	2	0.361	0.926	0.926	0.962	0.639
TP4	R34IU6_60_7Gy	1	0.290	0.889	0.889	0.943	0.710
TP4	R34IU6_60_7Gy	2	0.496	0.549	0.546	0.741	0.504
TP5	IU_VAGINA_7Gy	1	0.209	0.857	0.857	0.926	0.791
TP6	R30IU6_60_7Gy	1	0.255	0.973	0.972	0.986	0.745
TP6	R30IU6_60_7Gy	2	0.360	0.861	0.861	0.928	0.640
TP7	R30IU6_60_7Gy	2	0.384	0.883	0.883	0.940	0.616
TP8	R30IU6_60_7Gy	1	0.460	0.812	0.812	0.901	0.540
TP9	R30IU4_7Gy	1	0.318	0.549	0.549	0.741	0.682
TP10	R34IU66_7Gy	1	0.510	0.824	0.824	0.908	0.490
TP10	R34IU66_7Gy	2	0.217	0.984	0.982	0.992	0.783
TP11	R34IU6_60_7Gy	1	0.395	0.818	0.816	0.905	0.605

TP12	R30IU4_60_7Gy	1	0.147	0.964	0.921	0.982	0.853
TP13	R34IU66_60_7Gy	1	0.430	0.824	0.824	0.908	0.570
TP14	R30IU4_45_7Gy	1	0.302	0.922	0.922	0.960	0.698
TP15	Sorbo IU3_45_7Gy	1	0.304	0.828	0.819	0.910	0.696
TP16	R30IU4_60_7Gy	1	0.228	0.928	0.927	0.963	0.772
TP17	R30IU4_60_7Gy	1	0.474	0.812	0.812	0.901	0.526
TP18	R30IU6_60_7Gy	1	0.443	0.814	0.812	0.902	0.557
TP18	R30IU6_60_7Gy	2	0.320	0.894	0.884	0.945	0.680
TP19	R30IU66_7Gy	1	0.513	0.796	0.796	0.892	0.487
TP20	RING & TANDEM_7Gy	1	0.295	0.949	0.949	0.974	0.705
TP21	R34IU6_45_7Gy	1	0.299	0.962	0.962	0.981	0.701
TP21	R34IU6_45_7Gy	2	0.385	0.827	0.827	0.909	0.615
TP22	R30IU4_60_7Gy	1	0.318	0.878	0.877	0.937	0.682
TP22	R30IU4_60_7Gy	2	0.370	0.943	0.943	0.971	0.630
TP22	R30IU4_60_7Gy	3	0.398	0.874	0.874	0.935	0.602
TP23	R34IU66_7Gy	1	0.319	0.776	0.772	0.881	0.681
TP24	R34IU6_60_7Gy	1	0.310	0.882	0.882	0.939	0.690
TP24	R34IU6_60_7Gy	2	0.372	0.908	0.908	0.953	0.628
TP25	RING & TANDEM_7Gy	1	0.278	0.918	0.918	0.958	0.722
TP26	R34IU6_45_7Gy	1	0.359	0.811	0.811	0.901	0.641

TP27	RING & TANDEM_7Gy	1	0.209	0.857	0.857	0.926	0.791
TP28	R34IU60_60_7Gy	1	0.320	0.980	0.980	0.990	0.680

Table 2 shows the dose indices for the 2019 patients who were treated using an applicator with two catheters (needles). **Note:** The number of fractions indicate whether a patient had only 1 fraction or more than 1. CN, COIN, and CI generally had good values (i.e. close to ideal value of 1) while DHI and DNR had low values. Most values for CI were 0.9 implying that 90% of the target volume received the prescribed dose. Similarly, to CI, CN, and COIN are conformity indices and the result obtained shows conformity as most of the values are close to 1. DHI and DNR both have similar a concept, they both describe the dose homogeneity. DHI and DNR had low and high values respectively, indicating that the implant was of poor quality. DNR values were too high as optimal dose distribution in terms of dose uniformity is achieved at the minimum DNR value, which is set at 0.

Table 3: Calculated dose indices for 2019 patients treated with an applicator with more than two catheters.

TREATMENT PLAN No.	APPLICATOR TYPE/DOSE	No.of FRACTIONS	COIN	CI	CN	DHI	DNR
TP1	6 NEEDLES_5Gy	1	0.888	0.943	0.890	0.261	0.739
TP1	6 NEEDLES_5Gy	3	0.921	0.960	0.921	0.181	0.819
TP2	Utrecht 4 NEEDLES_7Gy	1	0.238	0.488	0.238	0.470	0.530
TP2	Utrecht 8 NEEDLES_7Gy	2	0.855	0.925	0.855	0.393	0.607
TP2	8 NEEDLES_7Gy	3	0.814	0.903	0.814	0.345	0.655

TP2	5 NEEDLES_7Gy	4	0.316	0.562	0.316	0.473	0.527
TP3	3 NEEDLES_5Gy	1	0.382	0.618	0.382	0.319	0.681
TP3	4 NEEDLES_5Gy	2	0.768	0.877	0.768	0.296	0.704
TP3	6 NEEDLES_5Gy	4	0.876	0.939	0.882	0.226	0.774
TP4	TANDEM & OVOID_7Gy	1	0.825	0.909	0.825	0.330	0.670
TP5	8 NEEDLES_7Gy	1	0.016	0.125	0.016	0.481	0.519
TP5	6 NEEDLES_7Gy	2	0.798	0.893	0.798	0.231	0.769
TP5	8 NEEDLES_7Gy	3	0.000	0.004	0.000	0.444	0.556

Table 3 shows the dose indices for 2019 patients who were treated using applicators with more than two catheters. Similarly, the same parameters were calculated for those patients with more than two catheters, and all of these patients had more than one fraction. DHI and DNR were seen not to improve for patients who had more than one fraction, but the CN, COIN, and CI improved. The values of DNR and DHI where generally low throughout. Ideal case would be to see an improvement in the values in the next fraction.

Table 4: Calculated dose indices for 2020 patients treated with an applicator with two catheters.

TREATMENT PLAN	APPLICATOR TYPE/ DOSE	No.of FRACTIONS	DHI	CN	COIN	CI	DNR
TP1	R26IU_60_9Gy	1	0.467	0.394	0.394	0.628	0.533
TP1	R26IU_60_9Gy	2	0.528	0.721	0.720	0.849	0.472
TP2	R34IU6_60_7Gy	1	0.406	0.811	0.810	0.900	0.594

TP2	R26IU6_60_7Gy	1	0.412	0.810	0.799	0.900	0.588
TP4	R30IU6_60_8Gy	1	0.496	0.431	0.431	0.656	0.504
TP4	R30IU6_60_8Gy	2	0.450	0.583	0.582	0.763	0.550
TP4	R30IU6_60_8Gy	3	0.363	0.802	0.777	0.895	0.637
TP5	RING & TANDEN_7Gy	1	0.567	0.520	0.520	0.721	0.433
TP6	R26IU6_60_7Gy	1	0.292	0.857	0.822	0.926	0.708
TP7	R26IU6_60_7Gy	1	0.422	0.866	0.866	0.931	0.578
TP8	RT_PELVIS_7Gy	1	0.435	0.496	0.495	0.704	0.565
TP9	R30IU6_60_7Gy	1	0.462	0.407	0.405	0.638	0.538
TP10	R26IU4_60_7Gy	1	0.000	1.000	0.949	1.000	1.000
TP11	R30IU6_60_7Gy	1	0.329	0.811	0.811	0.901	0.671
TP12	R34IU4_60_7Gy	1	0.332	0.776	0.764	0.881	0.668
TP12	R34IU4_60_7Gy	2	0.401	0.811	0.810	0.901	0.599
TP13	R30IU6_60_7Gy	1	0.441	0.813	0.809	0.902	0.559
TP14	RING & TANDEM_8Gy	1	0.431	0.847	0.847	0.920	0.569
TP15	RING & TANDEM_7Gy	1	0.507	0.614	0.614	0.784	0.493
TP16	RING & TANDEM_7Gy	1	0.442	0.544	0.522	0.737	0.558
TP17	R30IU6_60_8Gy	1	0.302	0.819	0.807	0.905	0.698
TP18	R26IU6_60_8Gy	1	0.425	0.818	0.817	0.905	0.575

TP19	RING & TANDEM_8Gy	1	0.330	0.701	0.697	0.837	0.670

Table 4 shows the dose indices for 2020 patients who were treated using applicators with two catheters.

Table 5: Calculated dose indices for 2020 patients treated with an applicator with more than two catheters

TREATMENT PLAN	APPLICATOR TYPE/DOSE	No.of FRACTIONS	COIN	CI	CN	DHI	DNR
TP1	Vienna R&T_ 7Gy	1	0.816	0.903	0.816	0.404	0.596
TP2	6 NEEDLES_7Gy	1	0.071	0.266	0.071	0.423	0.577
TP3	VIENNA R30IU60_60_7Gy	1	0.730	0.855	0.731	0.423	0.577
TP4	CYLINDER & NEEDLES_7Gy	1	0.641	0.810	0.656	0.399	0.601
TP5	5 NEEDLES_7Gy	1	0.578	0.764	0.583	0.327	0.673
TP5	9 NEEDLES_7Gy	2	0.834	0.918	0.842	0.463	0.537
TP5	9 NEEDLES_7Gy	3	0.838	0.916	0.839	0.299	0.701
TP6	IU+CYL+NEEDLE_7 Gy	1	0.825	0.908	0.825	0.417	0.583
TP6	IU+CYL+NEEDLE_7 Gy	2	0.716	0.848	0.719	0.511	0.489
TP6	IU+CYL+NEEDLE_7 Gy	3	0.353	0.594	0.353	0.456	0.544
TP7	5 NEEDLES_7Gy	1	0.371	0.609	0.371	0.463	0.537

TP8	CYL & NEEDLES_7Gy	1	0.755	0.870	0.756	0.332	0.668
TP8	CYL & NEEDLES_7Gy	2	0.595	0.774	0.598	0.402	0.598
TP8	CYL & NEEDLES_7Gy	3	0.598	0.775	0.601	0.440	0.560
TP8	CYL & NEEDLES_7Gy	4	0.800	0.895	0.801	0.280	0.720
TP9	5 NEEDLES_7Gy	1	0.132	0.363	0.132	0.504	0.496
TP10	4 NEEDLES_7Gy	1	0.005	0.071	0.005	0.510	0.490
TP11	INTERSTITIAL RING & NEEDLES_8Gy	1	0.613	0.783	0.613	0.400	0.600
TP12	7 NEEDLES_7Gy	1	0.833	0.913	0.833	0.482	0.518
TP13	10 NEEDLES_8Gy	1	0.799	0.898	0.806	0.435	0.565
TP13	10 NEEDLES_8Gy	2	0.701	0.841	0.706	0.375	0.625
TP14	4 NEEDLES_9Gy	1	0.005	0.071	0.005	0.510	0.490
TP15	OVOIDS & TANDEM_8Gy	1	0.619	0.787	0.619	0.407	0.593
TP15	OVOIDS & TANDEM_8Gy	2	0.256	0.506	0.256	0.568	0.432
TP16	12 NEEDLES_7Gy	1	0.884	0.940	0.884	0.294	0.706
TP16	9 NEEDLES_7Gy	2	0.811	0.901	0.812	0.274	0.726
TP16	10 NEEDLES_7Gy	3	0.820	0.907	0.822	0.301	0.699
TP16	3 NEEDLES_7Gy	4	0.000	0.016	0.000	0.588	0.413
TP17	9 NEEDLES_8Gy	1	0.105	0.324	0.105	0.481	0.519

TP17	9 NEEDLES_8Gy	2	0.347	0.589	0.347	0.428	0.572
TP17	9 NEEDLES_8Gy	3	0.766	0.876	0.767	0.353	0.647
TP17	9 NEEDLES_8Gy	4	0.109	0.331	0.109	0.487	0.513
TP18	3 NEEDLES_9Gy	1	0.070	0.265	0.070	0.493	0.507
TP19	4 NEEDLES_7Gy	1	0.094	0.306	0.094	0.494	0.506
TP19	7 NEEDLES_7Gy	2	0.772	0.881	0.776	0.423	0.577
TP19	7 NEEDLES_7Gy	3	0.863	0.929	0.863	0.370	0.630

Table 5 shows dose indices for 2020 patients who were treated using an applicator with more than two catheters. From Table 5, very few patients had a good value for COIN (i.e close to ideal value of 1 and the adopted threshold of 0.84). Similarly, CN and CI were very low for the majority of the patients indicating implants of low quality (non-conforming). DHI was generally low and the ideal value for DNR is 0 but from observations, the values were too large as most were above 0.50 implying than 50% of the target volume had non-uniform dose. The DNR is supposed to be 0 ideally because the dose coverage in the clinical target volume is expected to be uniform, hence non-uniformity is supposed to be minimized as much as possible so as to have a larger part of the CTV having uniform dose.

Table 6: Calculated dose indices for 2021 patients who were treated with an applicator with two catheters

TREATMENT PLAN	APPLICATOR TYPE/DOSE	No.of FRACTIONS	DHI	CN	COIN	CI	DNR
TP1	Sorbo IU_8Gy	1	0.464	0.558	0.552	0.747	0.536
TP2	R26IU60_60_8Gy	1	0.351	0.811	0.811	0.901	0.649
TP2	R26IU60_60_8Gy	2	0.353	0.794	0.794	0.891	0.647
	R26IU60_60_8Gy	3	0.450	0.680	0.680	0.825	0.550

TP3	R30IU60_60_8Gy	1	0.401	0.783	0.783	0.885	0.599
	R30IU60_60_8Gy	2	0.368	0.824	0.824	0.908	0.632
	R30IU60_60_8Gy	3	0.448	0.817	0.817	0.904	0.552
TP4	R30IU40_60_8Gy	1	0.417	0.827	0.826	0.909	0.583
	R30IU40_60_8Gy	2	0.346	0.811	0.811	0.901	0.654
TP5	R30IU60_60_8Gy	1	0.369	0.803	0.803	0.896	0.631
TP6	R26IU45_60_8Gy	1	0.339	0.811	0.810	0.900	0.661
	R26IU45_60_8Gy	2	0.380	0.707	0.706	0.841	0.620
	R26IU45_60_8Gy	3	0.329	0.757	0.753	0.870	0.671
TP7	R26IU60_40_8Gy	1	0.391	0.818	0.815	0.904	0.609
	R26IU60_40_8Gy	2	0.371	0.737	0.731	0.859	0.629
	R26IU60_40_8Gy	3	0.384	0.666	0.663	0.816	0.616
TP8	R34IU60_60_8Gy	1	0.490	0.665	0.665	0.815	0.510
	R34IU60_60_8Gy	2	0.432	0.833	0.833	0.913	0.568
	R34IU60_60_8Gy	3	0.457	0.752	0.752	0.867	0.543
TP9	R34IU60_60_8Gy	1	0.351	0.818	0.818	0.904	0.649
TP10	R30IU40_60_8Gy	1	0.269	0.796	0.766	0.892	0.731
	R30IU40_60_8Gy	2	0.317	0.820	0.820	0.906	0.683
	R30IU40_60_8Gy	3	0.268	0.800	0.800	0.894	0.732
TP11	R26IU40_60_8Gy	1	0.337	0.864	0.864	0.929	0.663
	R26IU40_60_8Gy	2	0.403	0.829	0.828	0.910	0.597
TP12	R30IU60_45_8Gy	1	0.504	0.775	0.775	0.880	0.496
	R30IU60_45_8Gy	2	0.369	0.839	0.838	0.916	0.631

TP13	R30IU60_60_8Gy	1	0.348	0.806	0.800	0.898	0.652
	R30IU60_60_8Gy	2	0.432	0.875	0.874	0.936	0.568
	R30IU60_60_8Gy	3	0.382	0.862	0.862	0.929	0.618
TP14	R30IU60_60_8Gy	1	0.373	0.891	0.891	0.944	0.627
	R30IU60_60_8Gy	2	0.328	0.833	0.830	0.913	0.672
	R30IU60_60_8Gy	3	0.368	0.844	0.844	0.919	0.632
TP15	R30IU60_60_8Gy	1	0.377	0.809	0.809	0.900	0.623
	R30IU60_60_8Gy	2	0.395	0.863	0.863	0.914	0.605
	R30IU60_60_8Gy	3	0.350	0.787	0.787	0.887	0.650
TP16	R26IU46_60_8Gy	1	0.337	0.806	0.805	0.898	0.663
	R26IU46_60_8Gy	2	0.375	0.770	0.770	0.878	0.625
TP17	R30IU60_60_8Gy	1	0.401	0.809	0.809	0.899	0.599
	R30IU60_60_8Gy	2	0.517	0.812	0.808	0.901	0.483
	R30IU60_60_8Gy	3	0.429	0.793	0.793	0.891	0.571
TP18	R26IU20_45_8Gy	1	0.240	0.743	0.742	0.862	0.760
	R26IU20_45_8Gy	2	0.403	0.810	0.810	0.900	0.597
	R26IU20_45_8Gy	3	0.344	0.811	0.809	0.900	0.656
TP19	R34IU60_60_8Gy	1	0.439	0.801	0.801	0.895	0.561
	R34IU60_60_8Gy	2	0.370	0.873	0.873	0.934	0.630
TP20	R26IU60_60_8Gy	1	0.441	0.816	0.816	0.903	0.559
	R26IU60_60_8Gy	2	0.347	0.920	0.920	0.959	0.653
	R26IU60_60_8Gy	3	0.398	0.823	0.822	0.907	0.602
TP21	R30IU40_60_8Gy	1	0.455	0.077	0.077	0.278	0.545

	R30IU40_60_8Gy	2	0.404	0.810	0.810	0.900	0.596
	R30IU40_60_8Gy	3	0.393	0.821	0.821	0.906	0.607
TP22	R30IU60_60_8Gy	1	0.349	0.819	0.816	0.905	0.651
	R30IU60_60_8Gy	2	0.297	0.802	0.797	0.896	0.703
	R30IU60_60_8Gy	3	0.363	0.744	0.744	0.863	0.637
TP23	R30IU60_60_8Gy	1	0.501	0.810	0.810	0.900	0.499
	R30IU60_60_8Gy	2	0.406	0.847	0.847	0.920	0.594
	R30IU60_60_8Gy	3	0.375	0.793	0.792	0.891	0.625
TP24	R30IU60_60_8Gy	1	0.387	0.760	0.760	0.872	0.613
	R30IU60_60_8Gy	2	0.330	0.819	0.819	0.905	0.670
TP25	R34IU60_60_8Gy	1	0.552	0.713	0.713	0.845	0.448
	R34IU60_60_8Gy	2	0.508	0.835	0.835	0.914	0.492
	R34IU60_60_8Gy	3	0.398	0.870	0.869	0.933	0.602
TP26	R30IU60_60_8Gy	1	0.359	0.842	0.842	0.918	0.641
	R30IU60_60_8Gy	2	0.386	0.781	0.780	0.884	0.614
	R30IU60_60_8Gy	3	0.376	0.817	0.789	0.904	0.624
TP27	R34IU60_60_5Gy	1	0.415	0.270	0.266	0.519	0.585
TP28	R34IU40_60_8Gy	1	0.389	0.696	0.695	0.834	0.611
	R34IU40_60_8Gy	2	0.442	0.867	0.867	0.931	0.558
TP29	R26IU60_60_8Gy	1	0.421	0.797	0.797	0.893	0.579
	R26IU60_60_8Gy	2	0.365	0.533	0.533	0.731	0.635
TP30	R30IU60_60_8Gy	1	0.449	0.886	0.885	0.942	0.551
	R30IU60_60_8Gy	2	0.439	0.813	0.813	0.902	0.561

	R30IU60_60_8Gy	3	0.538	0.791	0.790	0.889	0.462
TP31	R30IU60_45_8Gy	1	0.438	0.819	0.819	0.905	0.562
	R30IU60_45_8Gy	2	0.369	0.835	0.835	0.914	0.631
	R30IU60_45_8Gy	3	0.364	0.687	0.685	0.828	0.636
TP32	R30IU40_60_8Gy	1	0.301	0.926	0.926	0.962	0.699
	R30IU40_60_8Gy	2	0.461	0.820	0.820	0.906	0.539
	R30IU40_60_8Gy	3	0.445	0.835	0.835	0.914	0.555
TP33	R30IU60_60_8Gy	1	0.529	0.784	0.784	0.885	0.471
	R30IU60_60_8Gy	2	0.442	0.824	0.824	0.908	0.558
TP34	INCID_8Gy	1	0.251	0.955	0.952	0.977	0.749
TP35	R30IU60_60_8Gy	1	0.387	0.821	0.821	0.906	0.613
	R30IU60_60_8Gy	2	0.353	0.879	0.879	0.938	0.647
	R30IU60_60_8Gy	3	0.357	0.890	0.890	0.943	0.643
TP36	R34IU60_60_8Gy	1	0.415	0.883	0.883	0.940	0.585
	R34IU60_60_8Gy	2	0.404	0.814	0.814	0.902	0.596
	R34IU60_60_8Gy	3	0.397	0.843	0.843	0.918	0.603
TP37	R34IU60_60_8Gy	1	0.442	0.817	0.817	0.904	0.558
	R34IU60_60_8Gy	2	0.391	0.809	0.809	0.900	0.609
	R34IU60_60_8Gy	3	0.375	0.702	0.700	0.838	0.625
TP38	R30IU60_60_8Gy	1	0.385	0.829	0.826	0.911	0.615
	R30IU60_60_8Gy	2	0.335	0.842	0.842	0.918	0.665
	R30IU60_60_8Gy	3	0.547	0.752	0.752	0.867	0.453
TP39	R26IU60_60_8Gy	1	0.401	0.802	0.802	0.896	0.599

	R26IU60_60_8Gy	2	0.514	0.801	0.801	0.895	0.486
	R26IU60_60_8Gy	3	0.386	0.788	0.788	0.888	0.614
TP40	R30IU60_60_8Gy	1	0.436	0.675	0.674	0.821	0.564
	R30IU60_60_8Gy	2	0.433	0.777	0.776	0.881	0.567
	R30IU60_60_8Gy	3	0.403	0.819	0.819	0.905	0.597
TP41	R26IU6_60_8Gy	1	0.408	0.708	0.708	0.841	0.592
	R26IU6_60_8Gy	2	0.436	0.714	0.714	0.845	0.564
TP42	R30IU60_60_8Gy	1	0.431	0.813	0.813	0.902	0.569
	R30IU60_60_8Gy	2	0.482	0.813	0.812	0.902	0.518
	R30IU60_60_8Gy	3	0.328	0.878	0.878	0.937	0.672
TP43	R30IU60_60_8Gy	1	0.453	0.763	0.762	0.873	0.547
	R30IU60_60_8Gy	2	0.412	0.739	0.739	0.860	0.588
	R30IU60_60_8Gy	3	0.495	0.306	0.306	0.553	0.505
TP44	R26IU60_60_8Gy	1	0.435	0.725	0.725	0.852	0.565
	R26IU60_60_8Gy	2	0.420	0.822	0.822	0.907	0.580
	R26IU60_60_8Gy	3	0.435	0.747	0.746	0.864	0.565
TP45	R26IU60_60_8Gy	1	0.381	0.794	0.785	0.891	0.619
	R26IU60_60_8Gy	2	0.269	0.724	0.716	0.851	0.731

Table 6 shows dose indices for 2021 patients treated using an applicator with two catheters. Table 6 shows the 5 dosimetric indices for the patients in the year 2021. The calculated values for CN, CI, and COIN were very low, indicating absence of conformity. Again the ideal case is that for a plan to be said its conforming (i.e acceptable cervical implant) the indices for conformity and DHI are supposed to be of value 1. For this study, COIN, CN, CI and DHI are said to be conforming if

the values are equal to or greater than 0.80, 0.65, 0.95 and 0.50 respectively, while a value equal to or less than 0.30 is acceptable for DNR. DHI and DNR values were seen to be very low and too large respectively comparing them to their respective thresholds.

Table 7: Calculated dose indices for 2021 patients who were treated with an applicator with more than two catheters

TREATMENT PLAN	APPLICATOR TYPE/DOSE	No.of FRACTIONS	DHI	CN	COIN	CI	DNR
TP1	6F 200mm FLEXI	1	0.207	0.808	0.789	0.899	0.793
	6F 200mm FLEXI	2	0.453	0.001	0.001	0.034	0.547
	R30IU60_60_8Gy	3	0.424	0.854	0.853	0.924	0.576
TP2	R30IU60_60_2N_8Gy	1	0.330	0.822	0.822	0.906	0.670
	R30IU60_60_2N_8Gy	2	0.426	0.779	0.779	0.882	0.574
	R30IU60_60_2N_8Gy	3	0.291	0.801	0.801	0.895	0.709
TP3	4 NEEDLES 4_3cm	1	0.216	0.685	0.662	0.828	0.784
	4 NEEDLES 4_3cm	2	0.968	0.081	0.081	0.285	0.032
TP4	R30IU40_60_8Gy	1	0.309	0.640	0.626	0.800	0.691
	R30IU40_60_8Gy	2	0.319	0.799	0.796	0.894	0.681
	R30IU40_60_8Gy	3	0.367	0.867	0.867	0.931	0.633
TP5	R34IU60_60_3NEEDLES_8Gy	1	0.353	0.751	0.726	0.866	0.647
	R34IU60_60_3NEEDLES_8Gy	2	0.456	0.762	0.762	0.873	0.544

	R34IU60_60_3NEEDLES_8Gy	3	0.464	0.783	0.783	0.885	0.536
TP6	R34IU60_60_8Gy	1	0.412	0.692	0.692	0.832	0.588
	R34IU60_60_8Gy	2	0.466	0.210	0.210	0.459	0.534
	2_NEEDLES	3	0.477	0.244	0.244	0.494	0.523
TP7	R26IU60_60_8Gy	1	0.422	0.781	0.781	0.884	0.578
	R26IU60_60_8Gy	2	0.413	0.824	0.824	0.907	0.587
	R26IU60_60_8Gy	3	0.406	0.788	0.787	0.888	0.594
TP8	R26IU60_60_8Gy	1	0.512	0.430	0.430	0.656	0.488
	R26IU60_60_8Gy	2	0.358	0.486	0.484	0.697	0.642
TP9	R34IU60_60_8Gy	1	0.407	0.810	0.808	0.900	0.593
	R34IU60_60_8Gy	2	0.316	0.810	0.806	0.900	0.684
TP10	R30IU6_60_8Gy	1	0.374	0.755	0.738	0.869	0.626
	R30IU6_60_8Gy	2	0.371	0.802	0.789	0.896	0.629
TP11	2 NEEDLES_8Gy	1	0.589	0.001	0.001	0.038	0.411
	2 NEEDLES_8Gy	2	0.249	0.861	0.861	0.928	0.751
	2 NEEDLES_8Gy	3	0.333	0.839	0.837	0.916	0.667

Table 7. Shows the dose Metrices for 2021 for patients who were treated with an applicator with more than two catheters. CN, CI, and COIN generally had low values, a different outcome compared to the first 2 years. Majority of the treatment plans here had only few indices passing out of the 5 (i.e 3 or less). This implies that these treatment plans had poor conformity with larger volumes of the CTV receiving small amounts of the prescribed dose (i.e larger volumes irradiated were outside the clinical target volume). But a slight improvement was observed between two fractions for patients who had more than one fraction except the third fraction which had lower

values compared to the first and second fractions. The same observation is made for DHI and DNR as almost all the patients had low and high values respectively, indicating low homogeneity of the dose.

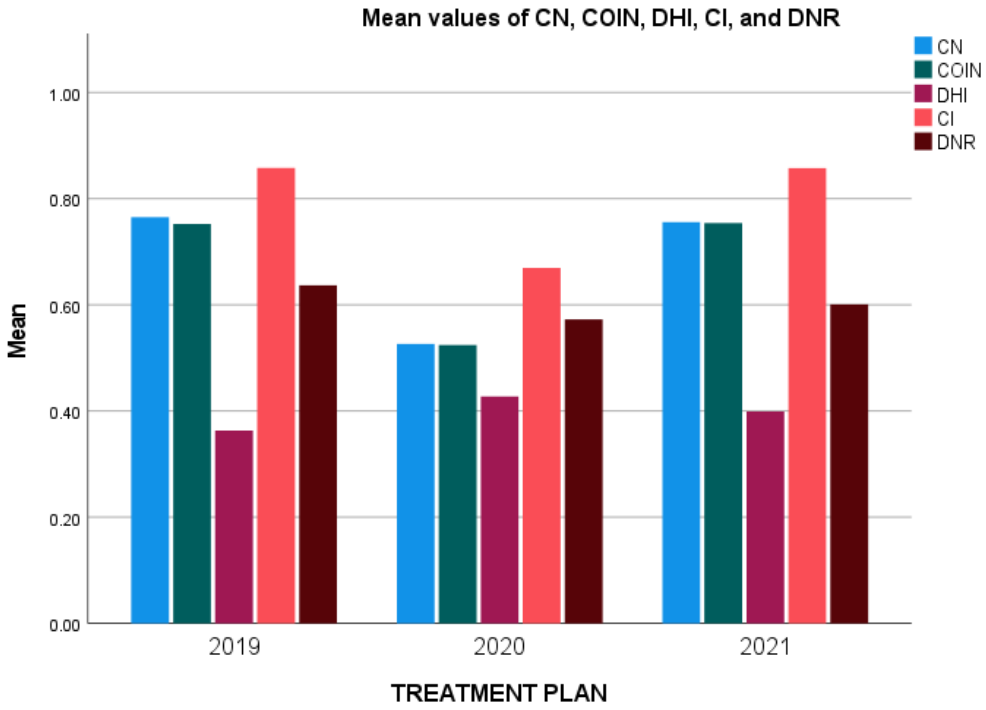

Figure 1: Mean values for the calculated dose indices

Figure 1 shows the mean values of the calculated dose indices across the 3 years (i.e. 2019 to 2021). For each year the average values for each index has been shown with 2019 treatment plans having better values for CN, COIN, and CI but very high DNR and lower DHI compared to the other years.

BLOCK DIAGRAM OF THE ALGORITHM

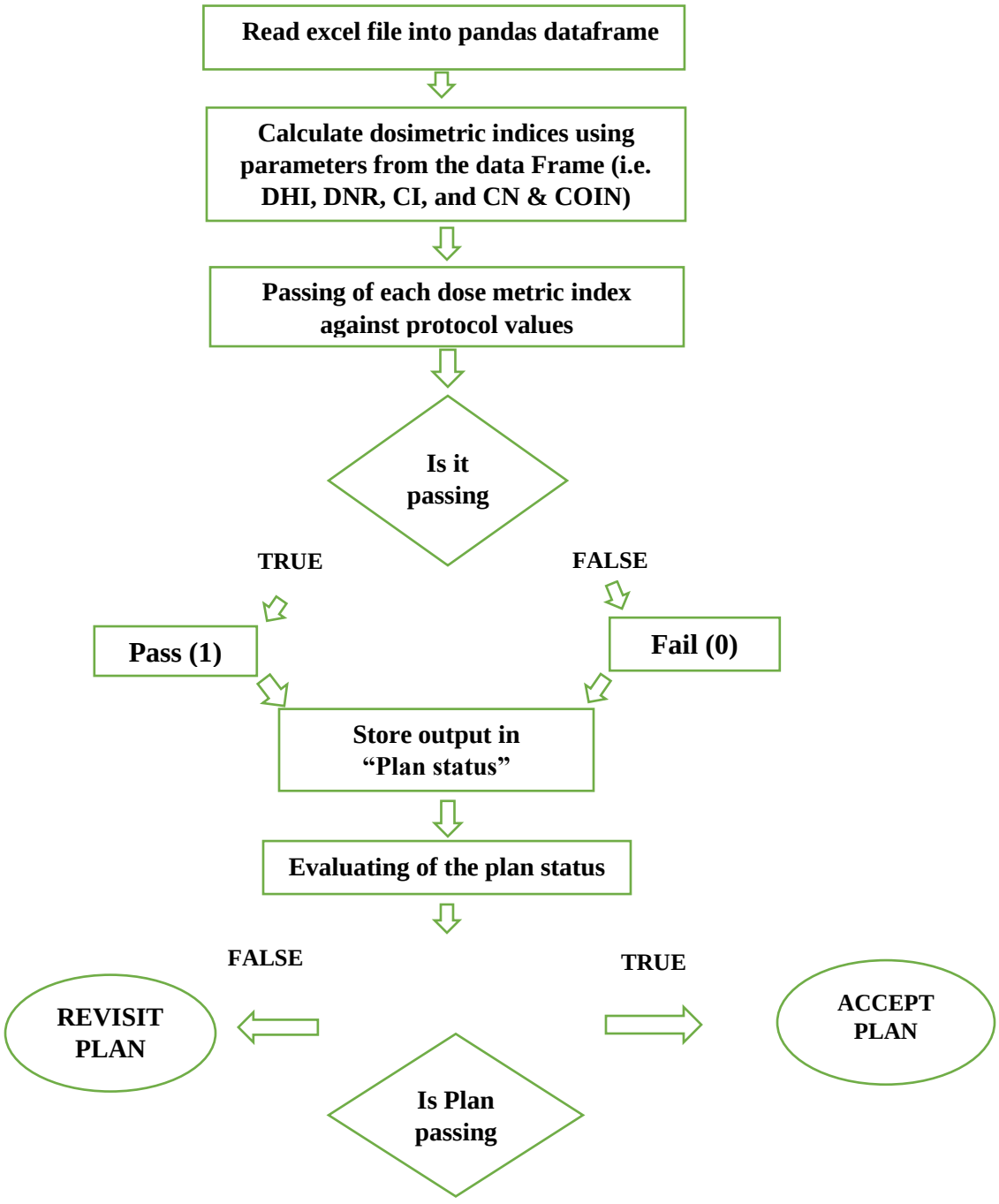

Figure 2: Block diagram of the Algorithm

Figure 2 shows a block diagram of the algorithm developed to pass or fail a treatment plan. The figure shows the block diagram of the developed algorithm to assess the quality of the plan using the calculated dose indices.

The algorithm was developed using 2021 cervical cancer treatment plans and it was also tested (i.e. run) for the datasets in 2019 and 2020. The general criteria that was set was such that 5 out 5 calculated dose indices had to pass for the treatment plan to pass.

The next table to be presented is a representation of the overall outcome from the algorithm. The algorithm developed automated the calculation of these dose indices and later used them to assess the treatment plans. The individual index state (e.g DHI state) is the output after weighing the index against the protocol value. A value of 1 representing a pass and a value of 0 representing a fail. The plan status indicates the overall plan state where the outcomes of the individual indices are summed up together. A treatment plan is said to be good (acceptable) if it has 5 indices passing out of the 5 while 4 or less out of 5 pass rate means that a plan has to be revisited.

Table 7: Dosimetric status and final plan status for 2020 Treatment Plans for Patients treated with an applicator with 2 catheters

TREATMENT PLAN	DHI State	CN State	COIN State	CI State	DNR State	TP State	plan status
TP1	0	0	0	0	0	0	FAIL
TP1	0	0	0	0	0	0	FAIL
TP2	0	1	0	0	0	1	FAIL
TP3	0	1	0	0	0	1	FAIL
TP4	0	0	0	0	0	0	FAIL
TP4	0	0	0	0	0	0	FAIL
TP4	0	1	0	0	0	1	FAIL
TP5	0	0	0	0	0	0	FAIL
TP6	0	1	0	0	0	1	FAIL
TP7	0	1	1	0	0	2	FAIL
TP8	0	0	0	0	0	0	FAIL
TP9	0	0	0	0	0	0	FAIL
TP10	0	1	1	1	0	3	FAIL
TP11	0	1	0	0	0	1	FAIL
TP12	0	0	0	0	0	0	FAIL
TP12	0	1	0	0	0	1	FAIL
TP13	0	1	0	0	0	1	FAIL
TP14	0	1	1	0	0	2	FAIL
TP15	0	0	0	0	0	0	FAIL
TP16	0	0	0	0	0	0	FAIL

TP17	0	1	0	0	0	1	FAIL
TP18	0	1	0	0	0	1	FAIL
TP19	0	0	0	0	0	0	FAIL

Table 7 above shows results obtained from the Python program. DHI State, CN State, COIN State, and DNR State are the outputs of each index (metric) once it has been compared with the protocol value (threshold value). 1 means the dose metric passed the protocol threshold while 0 means the dose metric did not pass the threshold. TP State is the total result of all 5 dose indices and lastly, the plan state is the interpretation of the TP state where status of the plan is indicating whether a plan passed or failed. None of the treatment plans are passing the set criteria (i.e 5 indices passing out the 5). From the results above, we see that majority of treatment plans only had 1 index passing out of the 5.

Table 8: Dosimetric status and final plan status for 2020 Treatment Plans for Patients who were treated with an applicator with more than 2 catheters

TREATMENT PLAN	DHI State	CN State	COIN State	CI State	DNR State	TP State	plan status
TP1	0	1	0	0	0	1	FAIL
TP2	0	0	0	0	0	0	FAIL
TP3	0	0	0	0	0	0	FAIL
TP4	0	0	0	0	0	0	FAIL
TP5	0	0	0	0	0	0	FAIL
TP5	0	1	0	0	0	1	FAIL
TP5	0	1	0	0	0	1	FAIL
TP6	0	1	0	0	0	1	FAIL
TP6	0	0	0	0	0	0	FAIL
TP6	0	0	0	0	0	0	FAIL

TP7	0	0	0	0	0	0	FAIL
TP8	0	0	0	0	0	0	FAIL
TP8	0	0	0	0	0	0	FAIL
TP8	0	0	0	0	0	0	FAIL
TP8	0	1	0	0	0	1	FAIL
TP9	0	0	0	0	0	0	FAIL
TP10	0	0	0	0	0	0	FAIL
TP11	0	0	0	0	0	0	FAIL
TP12	0	1	0	0	0	1	FAIL
TP13	0	1	0	0	0	1	FAIL
TP13	0	0	0	0	0	0	FAIL
TP14	0	0	0	0	0	0	FAIL
TP15	0	0	0	0	0	0	FAIL
TP15	0	0	0	0	0	0	FAIL
TP16	0	1	1	0	0	2	FAIL
TP16	0	1	0	0	0	1	FAIL
TP16	0	1	0	0	0	1	FAIL
TP16	0	0	0	0	0	0	FAIL
TP17	0	0	0	0	0	0	FAIL
TP17	0	0	0	0	0	0	FAIL
TP17	0	0	0	0	0	0	FAIL
TP17	0	0	0	0	0	0	FAIL
TP18	0	0	0	0	0	0	FAIL

TP19	0	0	0	0	0	0	FAIL
TP19	0	0	0	0	0	0	FAIL
TP19	0	1	1	0	0	2	FAIL
TP19	0	0	0	0	0	0	FAIL

Similarly, table 8 shows the final output of the Python program for patients treated with applicators with more than 2 catheters. As seen none of the treatment plans passed the set criteria. DNR values were very large compared to the acceptable threshold of ≤ 0.30. Similarly, DHI had low values of less than 0.50 for most of the plans implying that less than 50% of the target volume was receiving a homogeneous dose.

Table 9: Dosimetric status and final plan status for 2021 Treatment Plans for Patients who were treated with an applicator with 2 catheters

TREATMENT PLAN	DHI State	CN State	COIN State	CI State	DNR State	TP State	plan status
TP1	0	0	0	0	0	0	FAIL
TP2	0	1	0	0	0	1	FAIL
TP2	0	0	0	0	0	0	FAIL
TP2	0	0	0	0	0	0	FAIL
TP3	0	0	0	0	0	0	FAIL
TP3	0	1	0	0	0	1	FAIL
TP3	0	1	0	0	0	1	FAIL
TP4	0	1	0	0	0	1	FAIL
TP4	0	1	0	0	0	1	FAIL
TP5	0	1	0	0	0	1	FAIL
TP6	0	1	0	0	0	1	FAIL
TP6	0	0	0	0	0	0	FAIL
TP6	0	0	0	0	0	0	FAIL
TP7	0	1	0	0	0	1	FAIL
TP7	0	0	0	0	0	0	FAIL
TP7	0	0	0	0	0	0	FAIL
TP8	0	0	0	0	0	0	FAIL
TP8	0	1	0	0	0	1	FAIL
TP8	0	0	0	0	0	0	FAIL
TP9	0	1	0	0	0	1	FAIL

TP10	0	0	0	0	0	0	FAIL
TP10	0	1	0	0	0	1	FAIL
TP10	0	1	0	0	0	1	FAIL
TP11	0	1	1	0	0	2	FAIL
TP11	0	1	0	0	0	1	FAIL
TP12	0	0	0	0	0	0	FAIL
TP12	0	1	0	0	0	1	FAIL
TP13	0	1	0	0	0	1	FAIL
TP13	0	1	1	0	0	2	FAIL
TP13	0	1	1	0	0	2	FAIL
TP14	0	1	1	0	0	2	FAIL
TP14	0	1	0	0	0	1	FAIL
TP14	0	1	1	0	0	2	FAIL
TP15	0	1	0	0	0	1	FAIL
TP15	0	1	1	0	0	2	FAIL
TP15	0	0	0	0	0	0	FAIL
TP16	0	1	0	0	0	1	FAIL
TP16	0	0	0	0	0	0	FAIL
TP17	0	1	0	0	0	1	FAIL
TP17	0	1	0	0	0	1	FAIL
TP17	0	0	0	0	0	0	FAIL
TP18	0	0	0	0	0	0	FAIL
TP18	0	1	0	0	0	1	FAIL

TP18	0	1	0	0	0	1	FAIL
TP19	0	1	0	0	0	1	FAIL
TP19	0	1	1	0	0	2	FAIL
TP20	0	1	0	0	0	1	FAIL
TP20	0	1	1	1	0	3	FAIL
TP20	0	1	0	0	0	1	FAIL
TP21	0	0	0	0	0	0	FAIL
TP21	0	1	0	0	0	1	FAIL
TP21	0	1	0	0	0	1	FAIL
TP22	0	1	0	0	0	1	FAIL
TP22	0	1	0	0	0	1	FAIL
TP22	0	0	0	0	0	0	FAIL
TP23	0	1	0	0	0	1	FAIL
TP23	0	1	1	0	0	2	FAIL
TP23	0	0	0	0	0	0	FAIL
TP24	0	0	0	0	0	0	FAIL
TP24	0	1	0	0	0	1	FAIL
TP25	0	0	0	0	0	0	FAIL
TP25	0	1	0	0	0	1	FAIL
TP25	0	1	1	0	0	2	FAIL
TP26	0	1	1	0	0	2	FAIL
TP26	0	0	0	0	0	0	FAIL
TP26	0	1	0	0	0	1	FAIL

TP27	0	0	0	0	0	0	FAIL
TP28	0	0	0	0	0	0	FAIL
TP28	0	1	1	0	0	2	FAIL
TP29	0	0	0	0	0	0	FAIL
TP29	0	0	0	0	0	0	FAIL
TP30	0	1	1	0	0	2	FAIL
TP30	0	1	0	0	0	1	FAIL
TP30	0	0	0	0	0	0	FAIL
TP31	0	1	0	0	0	1	FAIL
TP31	0	1	0	0	0	1	FAIL
TP31	0	0	0	0	0	0	FAIL
TP32	0	1	1	1	0	3	FAIL
TP32	0	1	0	0	0	1	FAIL
TP32	0	1	0	0	0	1	FAIL
TP33	0	0	0	0	0	0	FAIL
TP33	0	1	0	0	0	1	FAIL
TP34	0	1	1	1	0	3	FAIL
TP35	0	1	0	0	0	1	FAIL
TP35	0	1	1	0	0	2	FAIL
TP35	0	1	1	0	0	2	FAIL
TP36	0	1	1	0	0	2	FAIL
TP36	0	1	0	0	0	1	FAIL
TP36	0	1	1	0	0	2	FAIL

TP37	0	1	0	0	0	1	FAIL
TP37	0	1	0	0	0	1	FAIL
TP37	0	0	0	0	0	0	FAIL
TP38	0	1	0	0	0	1	FAIL
TP38	0	1	1	0	0	2	FAIL
TP38	0	0	0	0	0	0	FAIL
TP39	0	1	0	0	0	1	FAIL
TP39	0	1	0	0	0	1	FAIL
TP39	0	0	0	0	0	0	FAIL
TP40	0	0	0	0	0	0	FAIL
TP40	0	0	0	0	0	0	FAIL
TP40	0	1	0	0	0	1	FAIL
TP41	0	0	0	0	0	0	FAIL
TP41	0	0	0	0	0	0	FAIL
TP42	0	1	0	0	0	1	FAIL
TP42	0	1	0	0	0	1	FAIL
TP42	0	1	1	0	0	2	FAIL
TP44	0	0	0	0	0	0	FAIL
TP44	0	0	0	0	0	0	FAIL
TP44	0	0	0	0	0	0	FAIL
TP45	0	0	0	0	0	0	FAIL
TP45	0	1	0	0	0	1	FAIL
TP45	0	0	0	0	0	0	FAIL

TP46	0	0	0	0	0	0	FAIL
TP46	0	0	0	0	0	0	FAIL

Table 9 shows results for the 2021 treatment plan for patients treated with an applicator with 2 catheters and results show a good number of these treatment plans barely had an index passing with majority recording only 1 index passing out of the 5. Again, this shows that these treatment plans had challenges in covering the clinical target volume with the prescribed dose, implying that a larger volume outside the CTV was irradiated and/or larger part of the volume had non-uniform dose distribution. Hence, DHI values were too small with very large values of DNR.

Table 10: Dosimetric status and final plan status for 2021 Treatment Plans for Patients who were treated with an applicator with more than 2 catheters

TREATMENT PLAN	DHI State	CN State	COIN State	CI State	DNR State	TP State	plan status
TP1	0	1	0	0	0	1	FAIL
TP1	0	0	0	0	0	0	FAIL
TP1	0	1	1	0	0	2	FAIL
TP2	0	1	0	0	0	1	FAIL
TP2	0	0	0	0	0	0	FAIL
TP2	0	1	0	0	0	1	FAIL
TP3	0	0	0	0	0	0	FAIL
TP3	1	0	0	0	1	2	FAIL
TP4	0	0	0	0	0	0	FAIL
TP4	0	0	0	0	0	0	FAIL
TP4	0	1	1	0	0	2	FAIL

TP5	0	0	0	0	0	0	FAIL
TP5	0	0	0	0	0	0	FAIL
TP5	0	0	0	0	0	0	FAIL
TP6	0	0	0	0	0	0	FAIL
TP6	0	0	0	0	0	0	FAIL
TP6	0	0	0	0	0	0	FAIL
TP7	0	0	0	0	0	0	FAIL
TP7	0	1	0	0	0	1	FAIL
TP7	0	0	0	0	0	0	FAIL
TP8	0	0	0	0	0	0	FAIL
TP8	0	0	0	0	0	0	FAIL
TP9	0	1	0	0	0	1	FAIL
TP9	0	1	0	0	0	1	FAIL
TP10	0	0	0	0	0	0	FAIL
TP10	0	1	0	0	0	1	FAIL
TP11	0	0	0	0	0	0	FAIL
TP11	0	1	1	0	0	2	FAIL
TP11	0	1	0	0	0	1	FAIL

Table 10 shows results for 2021 patients treated with applicators with more than 2 catheters and results show that none of the plans passed the set criteria. However, a few of the plans had only 1 index passing.

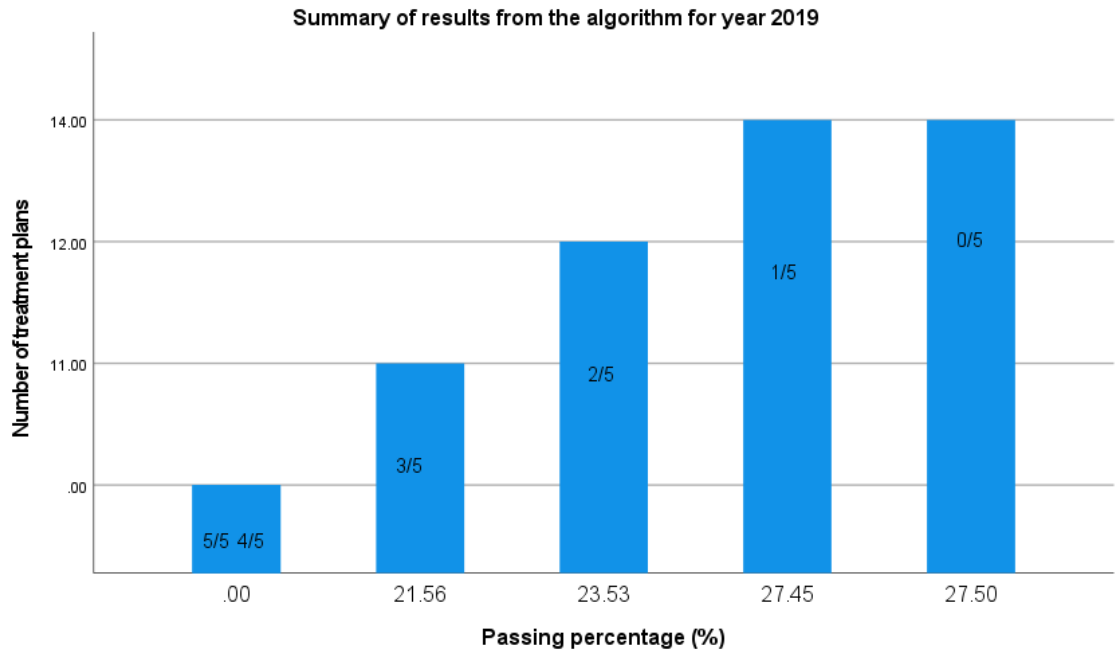

Figure 3: Summary of results from the Algorithm for the year 2019

Figure 3 shows statistics of the algorithm output for 2019; none of the treatment plans had either 5 or 4 indices passing out of the 5 calculated, representing 0% of the population. However, 11 of the treatment plans had at least 3 indices passing out of the five representing 21.56% of the total treatment plans, while 12 of the treatment plans had only 2 indices passing (i.e. 23.53%) while 14 plans had 1 index passing and another 14 plans had none of the index passing representing a population percentage of 27.45% and 27.5% respectively.

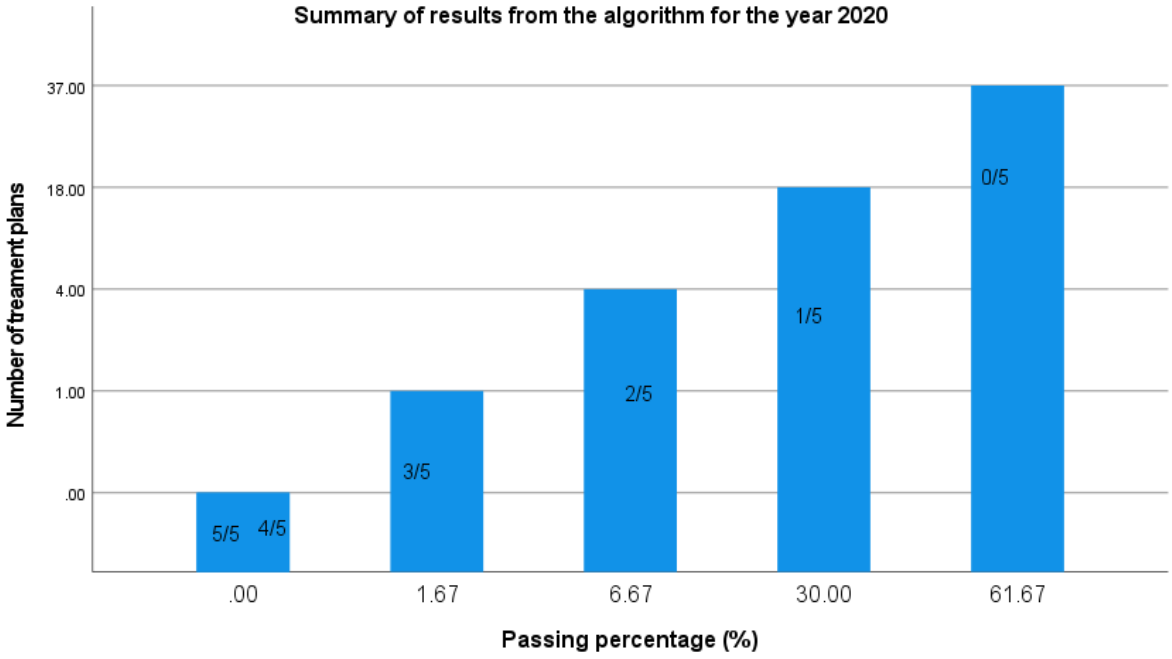

Figure 4: Summary of results from the Algorithm for the year 2020

Figure 4 shows the statistics of the results of the algorithm for the year 2020; no treatment plan had either 5 or 4 indices passing, representing 0% of the entire population for 2020. While 1 treatment plan had 3 of the indices pass (i.e. 1.67%) and 4 of these treatment plans had only 2 indices passing out of the 5 representing 6.67% of the population. 18 plans had only 1 index passing representing 30% of the treatment plans, and 37 plans had none of the indices passing representing 61.67% of the total treatment plans..

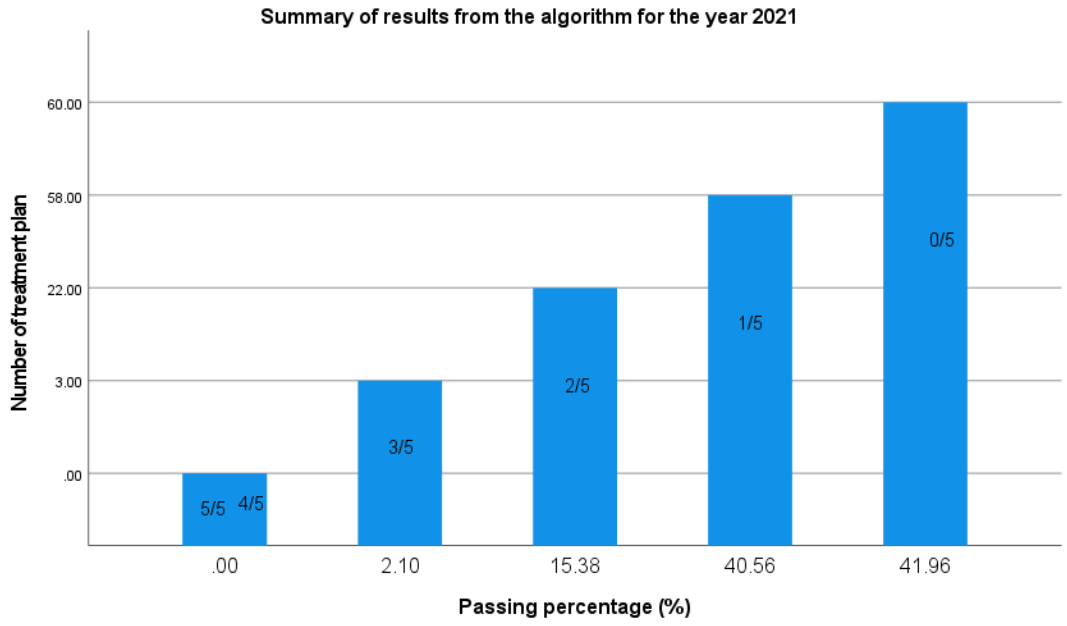

Figure 5: Summary of results from the Algorithm for the year 2021

Figure 5 shows statistics of the results from the algorithm for 2021; similarly, none of the treatment plans had either 5 or 4 indices passing representing a 0% of the entire population while 3 plans had only 3 indices passing, a representation of 2.10%. However, 22 of these plans had 2 indices passing representing a population of 15.38% while 58 plans only had one index passing a representation of 40.56% and 60 of the treatment plans had no index passing, representing a percentage of 41.96%.

4.3 Results from Statistical Analysis

2D scatter curves were plotted between the indices and the r-value (confidence interval: 95%) of these plots was obtained. Python was used to generate these relations after checking the correlations. The following plots where generated for the purpose of establishing how each of these indices affect each other.

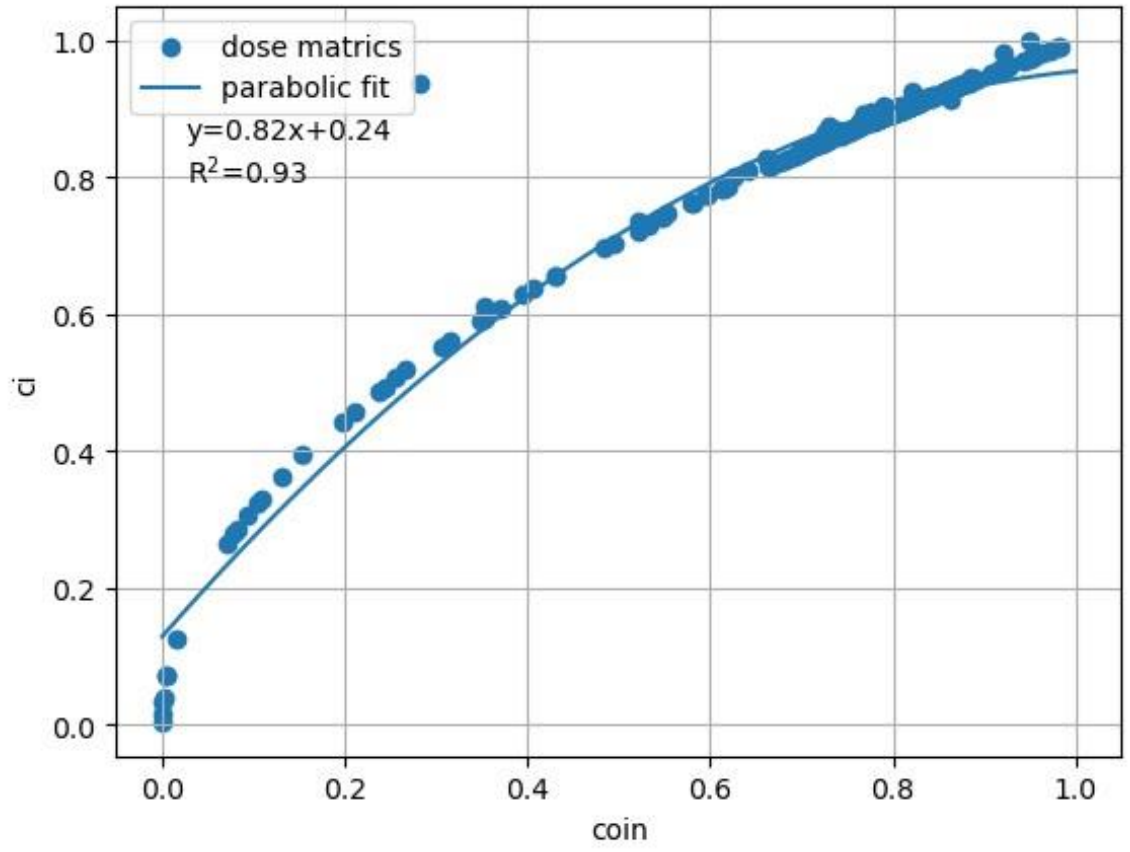

Figure 6: 2D scatter graph correlating between conformity index (COIN) and coverage index (CI)

The relationship of the plot of COIN and CI is shown in Figure 2. The plot indicates that CI increases in a parabolic trend as COIN increases. The slope of the curve was 0.82 implying a high rate of change of CI as COIN changes. The value of CI increases as COIN increases. The r-value between CI and COIN was +0.963, which was statistically significant with a confidence interval of 95%.

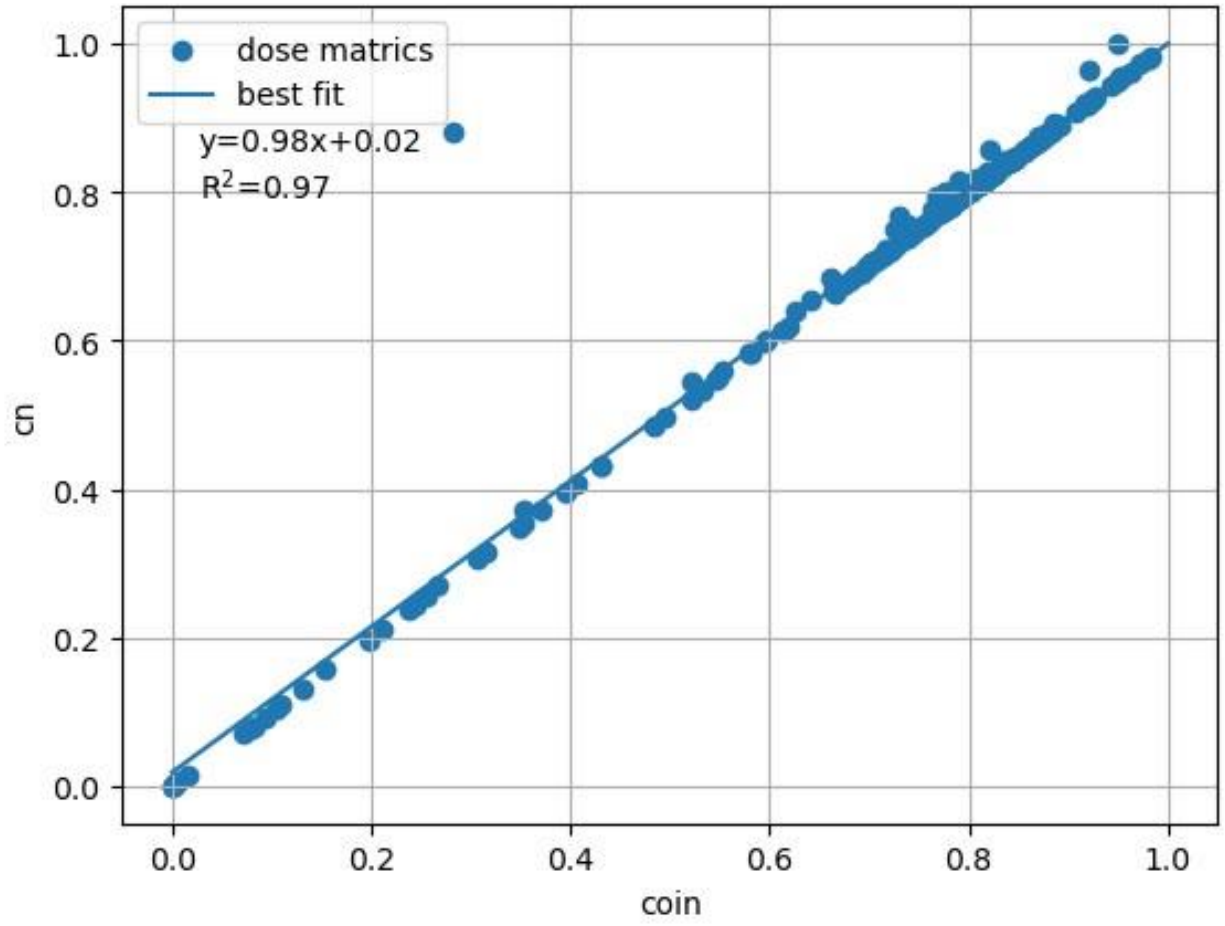

Figure 7:2D scatter correlating between conformity index (COIN) and conformity number (CN)

The relationship of the plot of COIN and CN is shown in Figure 3 and indicates that CN increases in a linear trend as COIN increases. The slope of the curve was 0.98 indicating a very high rate of change between the two values. The r-value between CN and COIN was +0.985, which was statistically significant with a confidence interval of 95%.

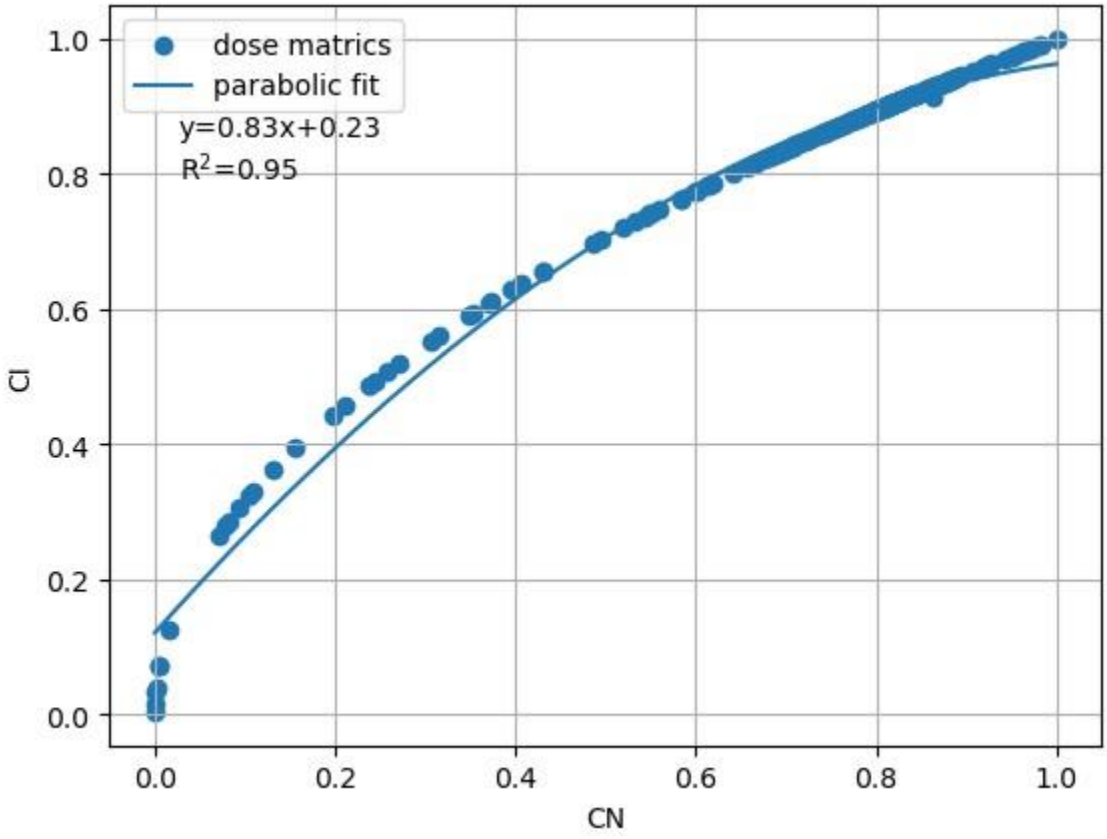

Figure 8: 2D scatter graph correlating between conformity number (CN) and coverage index (CI).

The relationship of the plot of CN and CI is shown in Figure 4 and indicates that CI increases in a parabolic trend as CN increases. The slope of the curve was 0.83. The r-value between CI and CN was +0.976, which was statistically significant with a confidence interval of 95%.

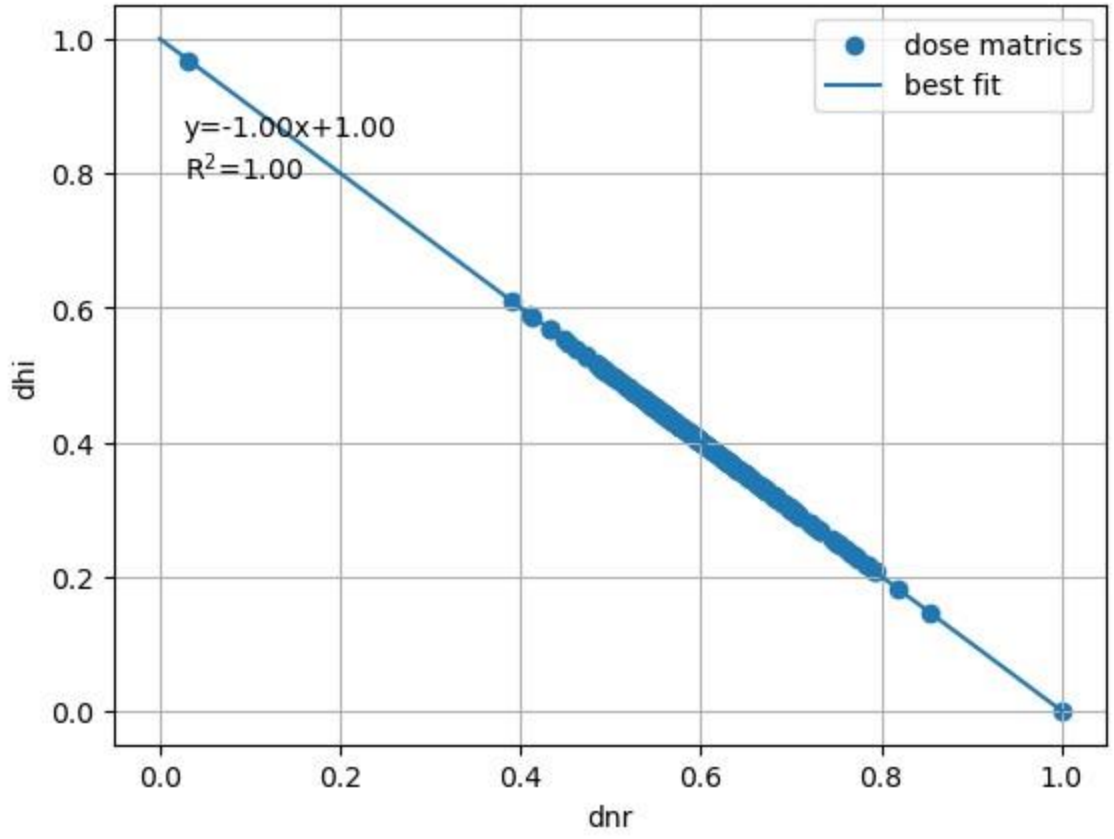

Figure 9: 2D scatter graph correlating between dose non-uniformity ratio (DNR) and dose homogeneity index (DHI).

The relationship of the plot of DHI and DNR is shown in Figure 5 and indicates that DNR increases in a linear trend as DHI decreases. The slope of the curve was -1.0 implying that as DNR increases DHI decreases. This outcome is very important because careful consideration is to be made when

trying to get both indices to pass as there is need to strike a balance. For a good cervical implant, DNR is supposed to be close to 0 while DHI is supposed to be 1. The r-value between DHI and DNR was -0.999, which was statistically significant with a confidence interval of 95%.

4.3 Summary

This chapter presents the results from the analyzed data. The various formulas used to calculate the dose indices are well explained in the previous chapter with their significance but the acceptable pass thresholds (protocol value) for each were highlighted. Quantitative comparative analysis with the standard values was used to check if current practices conformed to the standards by use of an algorithm, results are as seen in table 2 to 12. The results showing the calculated metrics showed that few of the plans had at least 3 indices passing out of the 5, while the majority only had 2 or 1 index passing. 108 of these treatment plans had no index passing a number that is quite significant. Lastly, a statistical analysis was done to assess the correlation of these indices. The least square method was employed using Python and scatter plots were generated indicating the r value. All the plots had a value of r greater than 0.9 which implied a very strong correlation of the indices. These plots assisted in establishing how these indices affect each other. A positive correlation was observed between the conformity indices while a strong negative correlation was seen between the homogeneity indices. The DNR increased as DHI reduced, whereas the ideal case should be high values of DHI and small values of DNR are to be expected.

CHAPTER 5

5.0 DISCUSSION

5.1 Introduction

The outcomes of this research have provided insight into how dose metric indices can be used to assess the quality of the treatment plan. However, the results should be interpreted with caution due to the limitations of the current research. This chapter discusses the results relating to the two objectives of the study namely, to calculate the dose metrics used in quality assurance and to develop and apply an algorithm using Python based on mathematical optimization that will determine whether the standard treatment plans that are being used are delivering adequate or correct dose. The outcomes of each objective are discussed respectively.

5.20 Evaluated values of dosimetric indices.

The selected dose metric indices were calculated for the three years, these being the dose Homogeneity Index (DHI), Dose Non-Uniformity Ratio (DNR), Conformity Index (COIN), Conformity Number (CN), and Coverage Index (CI). The values of these indices for the three years ranged from 0.34 to 0.43, 0.57 to 0.66, 0.52 to 0.86, 0.53 to 0.86, and 0.67 to 0.93 respectively. The year 2019 had better values for COIN, CN, and CI with their mean values; of 0.86, 0.86, and 0.93 respectively compared to the other years. These values agree with the outcomes from most similar studies done around the calculation of the dose indices. A study done by Major et. al [39] and Poddar et. al [32] found a value of 0.95 for CI and they do recommend this value for the acceptability of a good cervical implant. However, the value of 0.93 obtained from this study is not a major violation as it indicates that 93% of the target volume receives the prescribed dose. Similarly, the values of COIN and CN, 0.86 respectively, obtained from this study are within error margin of certified value of 1.This means that the plan encompasses 86% of the target volume. DNR and DHI values were high and low (i.e. ideal value is supposed to 0 and 1) respectively throughout all three years.

5.21 Outcome of the Algorithm

The aim of this study was to develop an algorithm that can assess the current practice in treatment planning at CDH by checking if the dose being delivered by standard BT treatment plans is optimal. In other words, the study aimed at ascertaining if what is being reported (i.e. using ICRU report) can be assessed through another parameter (i.e. use of dose indices) as a second check.

The algorithm was developed, and the results showed that none of the treatment plans passed the set criteria (i.e. 5 indices passing out of the 5). The dose metric threshold values used in this study are cited from different studies, a few of which categorically pointed out and recommended the values for the acceptability of good cervical implants. However, for most of these dose indices calculated, not much information is given on the acceptability thresholds. In such cases mean values that were close to conformity were adopted for this study. The following were the adopted thresholds for DHI, CN, COIN, and DNR; 0.50, 0.65, 0.80, 0.90 and 0.30 respectively. The dose metric threshold values selected may not be generic as they may depend on the implant site and are institution specific. Hence, the adopted values may not be conclusive, therefore, an institutional protocol can be made regarding the acceptability criteria of indices. This is to ensure uniformity among the users within the institution during the optimization process.

However, few of the plans had better values of the dose metrices with at least three indices passing. Ideal values for COIN, CI, and CN were recorded with their mean values being 0.86(±0.09), 0.93(±0.05), and 0.86(±0.09) respectively. This meant that the distribution of radiation conformed to the shape of the radio surgical target. None of the plans had an acceptable value for DHI and DNR with average values ranging from 0.34 – 0.43 and 0.57 – 0.66 respectively. This means that there is need to improve dose homogeneity within the target volume and to reduce the non-homogeneity within the target volume. It is evident from the results that the DNR value was big. This implies that only 43% or less of the target volume had a homogeneous dose distribution and a larger part of it (i.e. 66%) had a non-uniform dose distribution.

From the result so far, it is evident that dose indices can also be used to assess the treatment plan because they are good indicators clearly showing the dose being received by the clinical target volume. Therefore, this algorithm can be an efficient way of verifying dose distributions.

A study done by Jayakody [12], examined the requirement to confirm the optimal dose determined by TPS using an impartial testing technique to remove the possibility of the tumor site being under- or over-irradiated; this is also done as part of Quality Assurance (QA). Therefore, this Algorithm will serve as an institutional protocol devised for the acceptability criteria of a treatment plan at CDH.

5.22 Statistical analysis of the dose indices

The present study showed that the conformity indices have a strong correlation with each other. COIN vs CI and CN vs CI had a parabolic relationship while COIN vs CN had a strong positive linear correlation with an r-value greater than 0.9. DHI vs DNR had a strong negative linear correlation with an r-value equal to -1.

There could be more factors that are affecting the outcome of these indices. Due to limitation in accessing patients files with clinical data, these factors could be clinically related such as a patients stature and girth, disease stage etc. and as such, more studies should be done to evaluate the clinical data to assess why the indices are low or higher than the anticipated values (i.e. a value close to 1 for COIN, CI, CI and DHI, while a value close to 0 is ideal for DNR). A study by Kehwar et al. [40] confirmed that higher values of DNR (i.e. > 0) were related to higher normal tissue complications. Kataria et al. [41] emphasized in their study that DHI rises with increasing prescribed dose and falls with increasing goal volume. The results obtained from the scatter plots showed how each index influences the other, this information will be useful when trying to bring all the indices into passing thresholds while creating an acceptable plan.

A study done by Kaur [42] highlighted the scarcity and heterogeneous information available in the literature on the correlation between dosimetric indices, these being coverage index (CI), Conformity index (COIN), Conformity Number (CN), dose homogeneity index (DHI), overdose volume index (ODI), and dose non-uniformity ratio (DNR), some of which have been included in the present study. The results of the scatter plots will be an addition to the already existing knowledge and provide insight into how some of these indices correlate with each other.

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

6.0 Introduction

This chapter gives the conclusion and recommendations of the study, based on the findings and the discussion.

6.1 CONCLUSION

The selected dose indices were calculated for using the parameters collected. The mean values found for these indices with their standard deviations were as follows: DHI ranged from 0.34 ± 0.09 – 0.43 ± 0.84, while CN ranged from 0.53 ± 0.31 - 0.86 ± 0.09, COIN ranged from 0.59 ± 0.34 – 0.86 ± 0.09, CI ranged from 0.67 ± 0.28 – 0.93 ± 0.05, and DNR ranged from 0.57 ± 0.08 – 0.66 ± 0.09. The year 2019 had better conformity values compared to the other years with their mean values as follows; 0.86 for COIN and CN and 0.93 for CI. Throughout the three years, none of the treatment plans had good values for DHI and DNR implying that none of the treatment plans passed the set criteria.

When trying to achieve a good plan there should be careful consideration to have an optimum balance between these indices without increasing the dose to the tissues and organs at risk. This should be done while yielding maximum dose coverage on the clinical target volume. Results from this study indicate that none of the treatment plans passed the set criteria as most of the dose indices did not pass the respective individual thresholds (protocol values). However, despite CDH using ICRU report in reporting doses to the volumes, these indices can be another way of reporting/and or verifying doses to the volumes. Further, the study observed a correlation between the three conformity indices (i.e., COIN, CN, and CI) and the two homogeneity indices (DHI and DNR). The results are useful when determining indices that meet the thresholds. The correlation between the dose indices was found to be statistically significant (i.e the relationships between indices does exist) and results show the influence that the dose indices have on each other and how they can affect the outcome of the other indices.

6.2 RECOMMENDATIONS

The Cancer Diseases Hospital should consider the following recommendations:

i. Adopting the algorithm as part of their routine in checking plan quality using an independent means (i.e. a second check) in their treatment planning process.
ii. Further studies can be done to see how the DHI and DNR values can be improved whilst keeping the other indices in passing thresholds (i.e. passing thresholds can be adjusted when devising institutional protocol values). Secondly, dose distributions to the target volume can be revisited to adjust the outcome (i.e. the values of DHI and DNR).
iii. There is need to investigate why 2019 had better dose index values compared to the following two years (i.e. 2020 & 2021).
iv. The study has only focused on dosimetric analysis and is purely computational physics. Hence, further studies can be done by reviewing the clinical data to establish the factors that could be associated with the plans failing the set criteria of 5 indices passing out of the 5 (i.e. the disease stage, age etc.).
v. This work may be extended by adding other dose metric indices as this study only took into consideration five dose indices.

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APPENDIX

```
# Import libraries
import pandas as pd
import numpy as np

# Read excel into dataframe: df_tp_2021
df_tp_2021 = pd.read_excel("2021 PATIENTS.xlsx")

# Calculate Dose Homogeneity Index (DHI)
DHI = (df_tp_2021["V(PTV_100)"] - df_tp_2021["V(PTV_150)"]) / df_tp_2021["V(PTV_100)"]
df_tp_2021["DHI"] = DHI

# Calculate Conformity Number (CN)
CN = (df_tp_2021["V(PTV_100)"]/100) * (df_tp_2021["PTV ref"]/df_tp_2021["Totref"])
df_tp_2021["CN"] = CN

# Calculate Conformity Index (COIN)
COIN = df_tp_2021["CN"] * (1 - (df_tp_2021["V_OARref1_Bladder(%)"]/df_tp_2021["V_OAR1_Bladder[ccm]"])) * \
    (1 - (df_tp_2021["V_OARref2_Rectum(%)"]/df_tp_2021["V_OAR2_Rectum[ccm]"])) * \
    (1 - (df_tp_2021["V_OARref3_Sigmoid(%)"]/df_tp_2021["V_OAR3_Sigmoid[ccm]"])) * \
    (1 - (df_tp_2021["V_OARref4_Small bowel(%)"]/df_tp_2021["V_OAR4_Small bowel[ccm]"]))
df_tp_2021["COIN"] = COIN

# Calculate Coverage Index (CI)
CI = df_tp_2021["V(PTV_100)"]/100
df_tp_2021["CI"] = CI

# Calculate Dose Non-Uniformity Ratio (DNR)
DNR = df_tp_2021["V(PTV_150)"] / df_tp_2021["V(PTV_100)"]
```

```
df_tp_2021["DNR"] = DNR

# Passing individual indices by comparing them against protocol values
df_tp_2021["DHI State"] = (df_tp_2021["DHI"] >= 0.50).astype(int)
df_tp_2021["CN State"] = (df_tp_2021["CN"] >= 0.65).astype(int)
df_tp_2021["COIN State"] = (df_tp_2021["COIN"] >= 0.80).astype(int)
df_tp_2021["CI State"] = (df_tp_2021["CI"] >= 0.90).astype(int)
df_tp_2021["DNR State"] = (df_tp_2021["DNR"] <= 0.30).astype(int)

# Passing of a treatment plan
df_tp_2021["TP State"] = df_tp_2021["DHI State"] + df_tp_2021["CN State"] + df_tp_2021["COIN State"] + \
                    df_tp_2021["CI State"] + df_tp_2021["DNR State"]

# Create a new dataframe with TP State column
df = df_tp_2021["TP State"].to_frame()

# Apply lambda function to categorize PASS/FAIL based on TP State
ans = df["TP State"].apply(lambda x: 'PASS' if x == 5 else 'FAIL').to_frame()

# Save the updated dataframe to an Excel file
df_tp_2021.to_excel("2021 PATIENTS.xlsx")
```

ETHICAL CLEARANCE

THE UNIVERSITY OF ZAMBIA

DIRECTORATE OF RESEARCH AND GRADUATE STUDIES

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APPROVAL OF STUDY

IORG No. 0005376
HSSREC IRB No. 00006465

6th October, 2022

REF NO. NASREC-2022-MAY-004

Ms. Mannah Kaniini
The University of Zambia,
School ofNatural Sciences,
P.O. Box 32379, LUSAKA.

Dear Ms. Kaniini,

RE: "OPTIMIZATION OF HIGH DOSE RATE BRACHYTERAPY TREATMENT PLAN USING AN ALGORITHM.

Reference is made to your protocol dated as captioned above. NASREC resolved to approve this study and your participation as Principal Investigator for a period of one year.

REVIEW TYPE	ORDINARY REVIEW	APPROVAL NO. NASREC-2022-MAY.-004
Approval and Expiry Date	Approval Date: 6th October, 2022	Expiry Date: 5th October, 2023
Protocol Version and Date	Version - Nil.	5 th October, 2023
Information Sheet, Consent Forms and Dates	English,	To be provided
Consent form ID and Date	Version – Nil	To be rovided
Recruitment Materials	Nil	Nil
Other Study Documents	Questionnaire.	