**Artigo Original**

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# Dwell time in the uterus and vagina as a parameter to analyze the dose distribution in cervix carcinoma for brachytherapy with Co-60 source. Clinical cases.

## Tempo de permanência no útero e na vagina como parâmetro para analisar a distribuição da dose no carcinoma do colo uterino para braquiterapia com fonte de Co-60. Casos clínicos.

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**Abstract**

Intracavitary gynecological brachytherapy uses as a guideline for dose distribution, the ratio between the pear length in the three directions of the axes considers at ICRU 38. The ratios h/w, h/t function as a parameter to find out how the uterus and vagina are covered by the prescription dose. This work correlates these ratios with the dwell times inside the uterus (tu) and vagina (tv) expecting to identify these times as criteria for the dose shape distribution. We performed an optimized treatment planning for 120 sessions of 6.0 Gy each, following the recommendations of the ABS, ICRU 38, and 89. The planning system used is HDRplus 3.0.4 with an HDR Eckert y Ziegler BEBIG Co0.A86 brachytherapy unit with Cobalt 60. Considering the tandem time modulation and the time differences between left and right irradiation in the vagina, the variation of the correlation with the number of sessions for the tu/tv ratio with h/w and h/t was studied. A correlation has been found between tu/tv with h/w and h/t, which depends on the amount of data. There is a good correlation between the tu/tv ratio with h/w and h/t respectively, which is stronger for the first one.

**Keywords**: Brachytherapy; dose distribution; intracavitary treatment, cervix neoplasm, optimization.

**Resumo**

*A braquiterapia ginecológica intracavitária usa como parâmetro para a distribuição da dose a relação entre o comprimento da pêra nas direções dos três eixos em relação à ICRU 38. A relação h/w, h/t nos dá um parâmetro para calcular como o útero e a vagina são cobertos. Este trabalho correlaciona estas proporções com os tempos de permanência dentro do útero (tu) e da vagina (tv), com a intenção de saber se podemos usar estes tempos como parâmetros para a distribuição da forma da dose. Foi feito um planejamento de tratamento otimizado para 120 sessões de 6.0 Gy cada uma, seguindo as recomendações da ABS, a ICRU 38 e 89. O sistema de planejamento utilizado é o HDRplus 3.0.4 com uma máquina de braquiterapia HDR Eckert y Ziegler BEBIG Co0.A86 com Cobalto 60. Tendo em conta a modulação do tempo em tandem e as diferenças de tempos entre a irradiação esquerda e direita na vagina, foi estudada a variação da correlação com o número de sessões para a relação tu/tv com h/w e h/t. Foi encontrada uma correlação entre tu/tv com h/w e h/t, e depende do número de dados. Existe uma boa correlação entre a relação tu/tv com h/w e h/t, respectivamente, que é mais forte para a primeira.*

**Palavras-chave**: *Braquiterapia; distribuição de doses; tratamento intracavitário; neoplasma do colo uterino; otimização.*

### 1. Introduction

The success of endocavitary brachytherapy in the treatment of cervical cancer depends on the application of curative doses delivered directly to the tumor with low doses delivered to healthy tissues such as the bladder, rectum, and small bowel (1,2,3).

High dose rate (HDR) brachytherapy in recent decades use treatment planning based on 2D and 3D imaging (computed tomography (CT) and/or magnetic resonance imaging (MRI)) and dose distribution optimization methods to ensure that the prescribed dose is delivered at treatment sites while reducing the risk of overdosing to critical organs (3,4).

Efficient optimization requires several dose definition points to allow for sufficient dose distribution across the dwell time at the different applicator stops. Non-use optimization needs dwell times and distances to be equal (5).

Optimization algorithms do not always produce dwell times with a uniform distribution, sometimes resulting in points with a high dose that can affect healthy tissue. This is mainly due to the surrounding anatomical modification or displacement of the applicator. Thus, optimization algorithms have incorporated a permanence time modulation system as an effort to homogenize them (4).

The metric properties used in treatment planning, necessary for the optimization and calculation of the reference volume, are width (w), thickness (t), and a maximum height (h) of the endocavitary source (6).

Previous studies have shown that modification of the dwell times and dwell positions of uterine and vaginal sources, using equal time and distances, results in different dose distribution for irradiations administered with Ir-192 source equipment (5). Subsequently, it was carried out with the same considerations for the Co-60 source (9).

This work aims to determine whether it is possible to find a correlation between the ratios of h/w and h/t with dwell times in the uterus and vagina when a pear shape is performed by a planning optimization. This work considers clinical cases with various anatomies for the treatment of cervical cancer administered with Co-60 source.

## 2. Materials and Methods

T This is a retrospective study of brachytherapy with 120 treatment sessions for 30 patients with gynecological cancer who were re-planned following the recommendation of ABS, ICRU 38, and ICRU 89. Patients were treated with a tandem and ring applicator. The treatment device was an HDR afterloading Eckert & Ziegler MultiSource® with Cobalt 60 source. The planning was performed with an HDRplus, version 3.0.4. For each session, the dose has been optimized by the "auto dwell time determination" algorithm using X-ray based planning. The corresponding step source is 5.0 mm for the uterus and vagina.

E Each plan contains the ABS points, and we use inverse planning to obtain a prescribed dose of 6.0 Gy at these points. The ABS points are placed 1.8 cm first and the others 2.0 cm from the tandem to the side (Figure 1).

Each session was administered with 6.0 Gy at point A. The treatment planning was done to maintain the position of the applicator and tandem in the midline of the patient. The size and angle of the applicator used in all treatments depended on the patients' anatomy. Orthogonal X-rays were used to reconstruct the position of the applicators in the TPS. The positions of the sources and the dwell times got after optimization have been recorded. It was calculated the extension of the pear along with the tandem as h, also the transversal long of the pear as w in the right-left direction, perpendicular at the tandem as t in the anterior-posterior direction at the sagittal oblique plane. The total dwell time source in the tandem is called tu, and tv is the whole dwell time in the ring (vagina), divided into tvl and tvr for left and right side as well, so tv is a sum of tvl and tvr.

In utero, time modulation was quantified for M (equation 1). This value takes into account all the dwell times in tandem steps. First, we calculated M for each session. Subsequently, we arranged the sessions from the highest to lowest M value. Keeping this order, we organized the 120 sessions by sets. First set, the 120 sessions; the second set, 119 sessions with the lowest value of M; third set, 118 sessions with the lowest value of M, and so on until we reach 30 sessions.

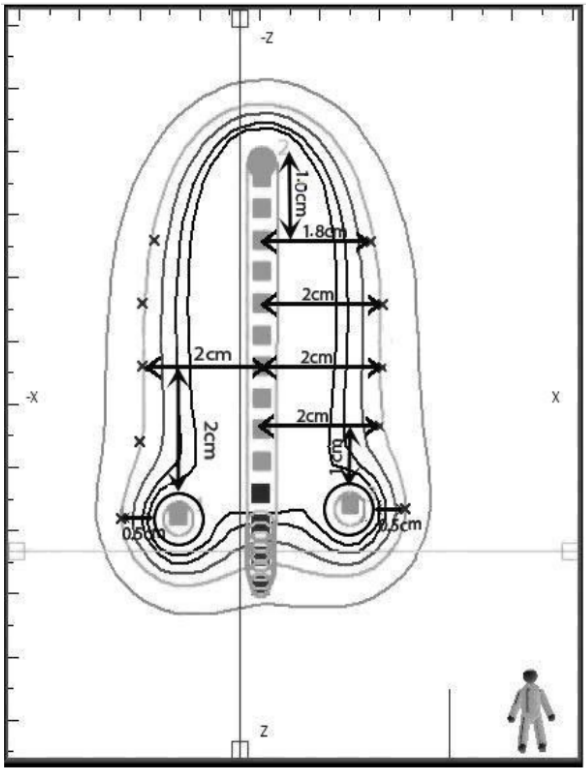


**Figure 1:** Coronal representation of the optimization points.

$$M = \frac{standard\ deviation(tu_i)}{average\ (tu_i)} \quad (1)$$

Statistical analysis was performed with SPSS software.

A correlation between the ratio (tu/tv) with the ratios (h/w) and (h/t) was calculated. Spearman's correlation was applied, and its statistical significance was calculated. We did this for all sets arranged above. We did this process to understand the behavior of the correlation with the number of sessions when M becomes smaller.

The dose distribution in the vagina depends on the time in this location. For example, if the time is similar on both sides of the ring, the symmetry of the pear shape is identified. The DIF relationship was defined to comprehend the implication of the times on both sides (equation 2).

$$DIF = \frac{|tvl - tvr|}{(tvl + tvr)/2} * 100 \quad (2)$$

We arranged all sessions in a second stage using DIF, from highest to lowest value in this order. Spearman's correlation was calculated for the first group and the 120 treatment sessions. The second group ranged from second to the 120th position, the third group ranged from third to the 120th position, and so on, until 30 sessions were reached. The Spearman correlation calculated was between the ratios (tu/tv) with the proportions (h/w) and (h/t).

Taking into account the correlation results, we used linear and quadratic regression to adjust the relationship of the variables (tu/tv) with (h/w) and (h/t).

## 3. Results

Optimization of the planning allows each treatment session to be stopped when the prescribed dose is reached. Figure 2 shows the distribution of the time spent in the uterus at each step for all sessions.

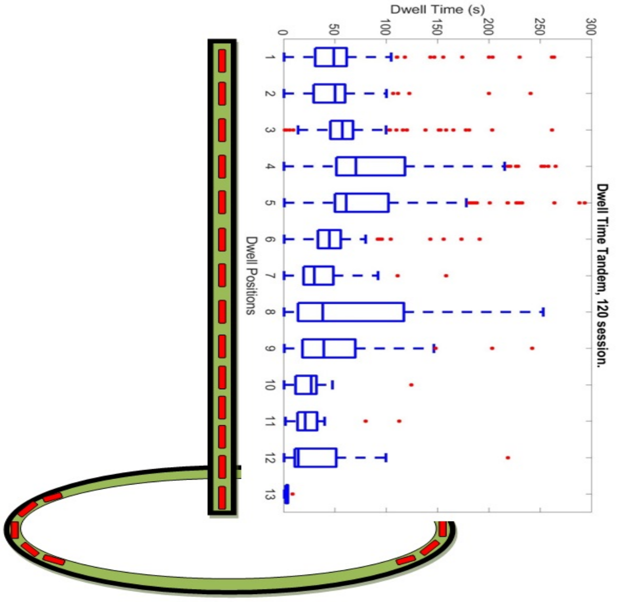


**Figure 2.** Tandem dwell time distribution in 120 sessions

The group with the lowest modulation in the uterus is represented in figure 3. This group corresponds to the 30 treatment sessions with the lowest M value.

The variables were derived from an abnormal distribution when analyzing the variables tu/tv, h/w, and h/t with the Kolmogorov-Smirnov test.

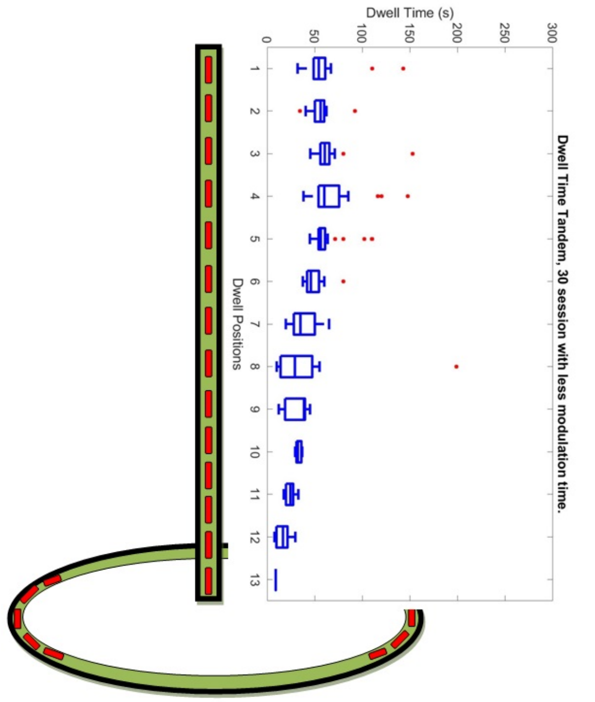


**Figure 3.** Dwell time tandem for 30 patients with less modulation

The Spearman correlation for the ratios: tu/tv between h/w and h/t is shown in figure 4 and figure 5, respectively. The figure is organized from highest to lowest M.

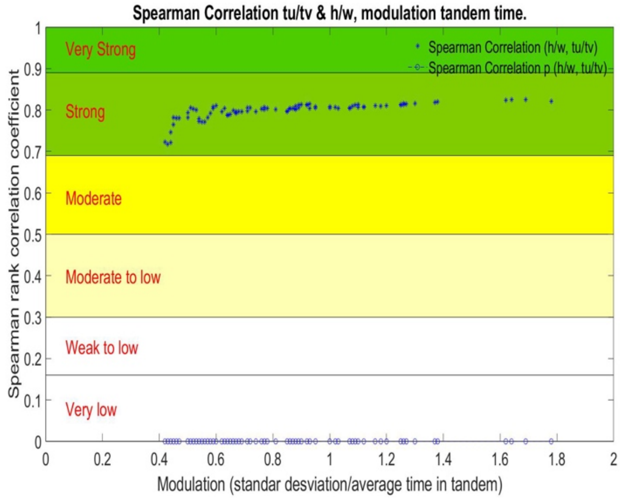


**Figure 4.** Uterus correlation tu/tv & h/w organized for time modulation in the uterus.

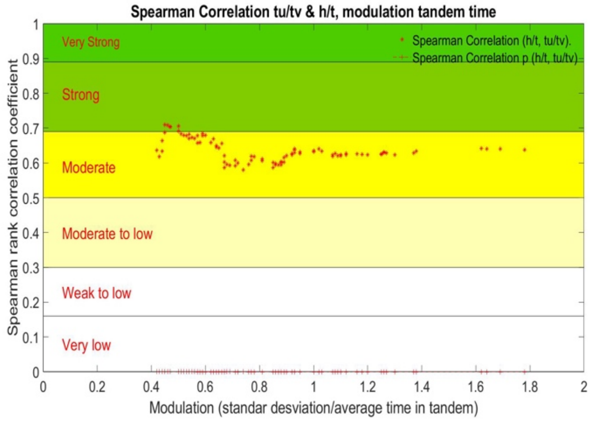


**Figure 5.** Uterus correlation tu/tv & h/t organized for time modulation in the uterus.

The distribution of time over 120 sessions for any stepping dwell time on the left side of the vagina is shown in Figure 6.

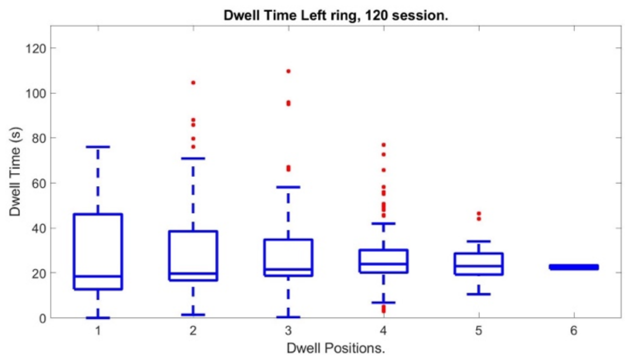


**Figure 6.** Dwell time in the ring for the left side in vagina.

Figure 7 presents the time distribution in 120 sessions for any stepping dwell time on the right side of the vagina.

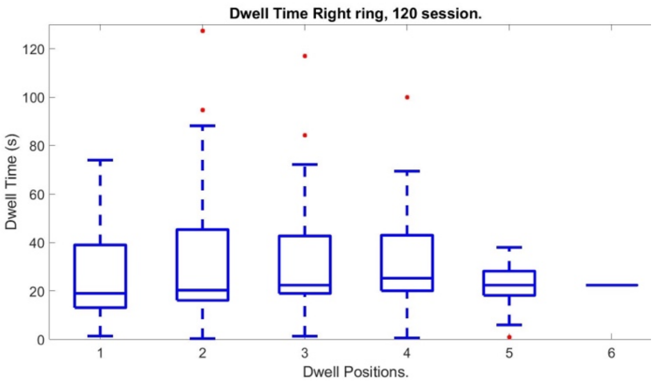


**Figure 7.** Dwell time in the ring for the right side in vagina

The group with the minor time difference on both sides of the vagina is shown in figure 8 (left side) and figure 9 (right side). This group had 30 treatment sessions with the lowest DIF value (equation 2).

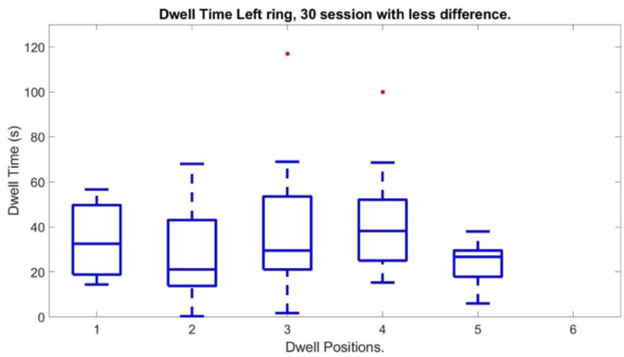


**Figure 8.** Dwell time in the ring for the left side in vagina, for 30 patients with less DIF.

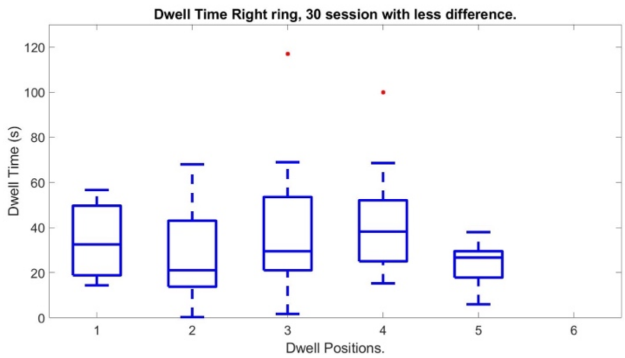


**Figure 9.** Dwell time in the ring for the right side in the vagina, for 30 patients with less DIF.

The planning optimization process provides different dwell times for any given step. The treatment sessions had 14 possible step positions in the uterus; any of this had its own dwell time. Although any plan has all these step possibilities, in the end, with the optimization, we obtained 16 sessions that have between 10-13 steps with dwell time. The average number of steps in the 120 sessions was 7.

A Spearman correlation organized by DIF value (equation 2) was calculated between right and left for h/w and tu/tv (Figure 10), as well as for h/t and tu/tv (Figure 11). It was arranged from highest to lowest DIF. These figures show the correlation for the 90 highest DIF.

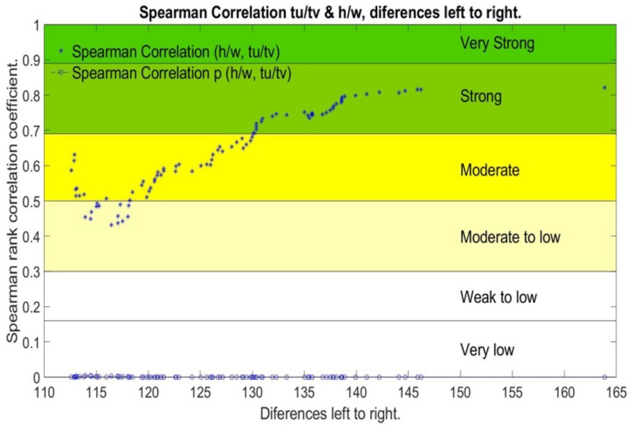


**Figure 10.** Correlation h/w & tu/tv organized for time difference on the left and the right side of the vagina.

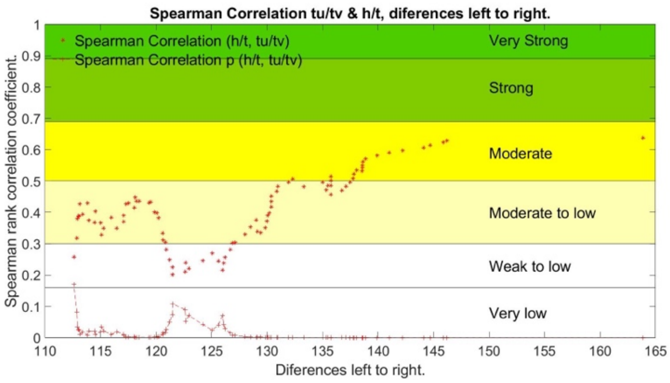


**Figure 11.** Correlation h/t & tu/tv organized for time difference on the left and the right side of the vagina.

A scatterplot is presented to show the correlation between the tu/tv ratio with h/w (Figure 12); this figure has a 95% confidence region with a linear fitting equation. We obtained an R square value of 0.6645. The fit is also possible when fitting the variables with a squared polynomial equation (Figure 13) for a 95% confidence region, with an R square value of 0.6834.

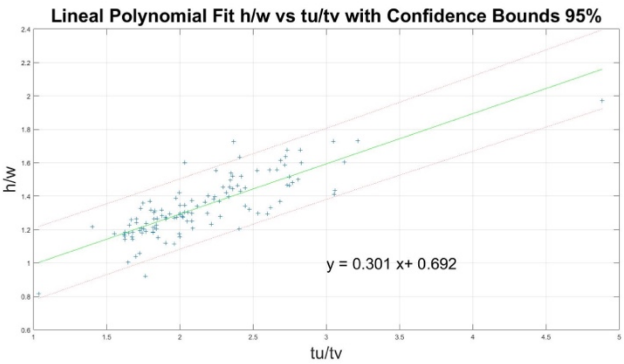


**Figure 12.** Scatterplot of h/w and tu/tv. Linear fit with a 95 % confidence region.

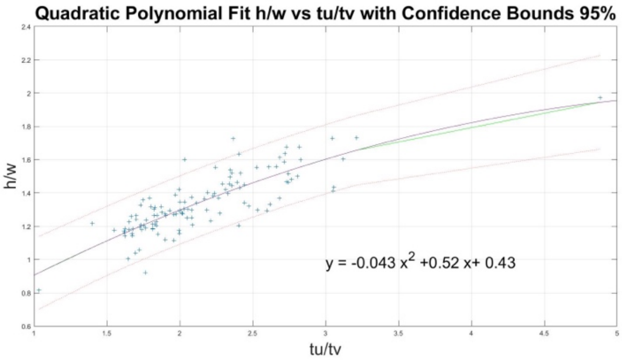


**Figure 13.** Scatterplot of h/w and tu/tv. Squared polynomial fit with 95 % confidence region.

A scatterplot for tu/tv with h/t with a linear fit equation had an R square value of 0.4962. Figure 14 shows these data with 95% confidence region bounded for the top and bottom lines. Moreover, the squared polynomial equation was also fitted for a 95% confidence region, it shows in Figure 15, the R square value was 0.5281.

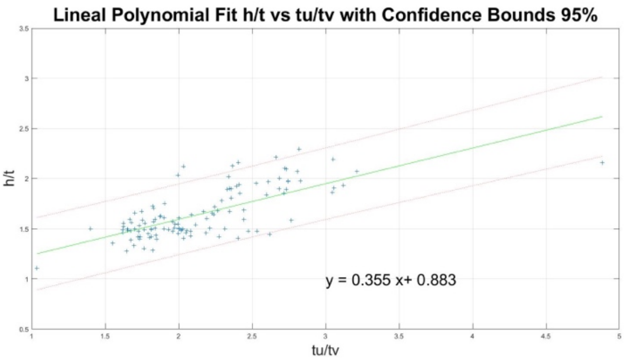


**Figure 14.** Scatterplot of h/t and tu/tv. Linear polynomial fit with a 95 % confidence region.

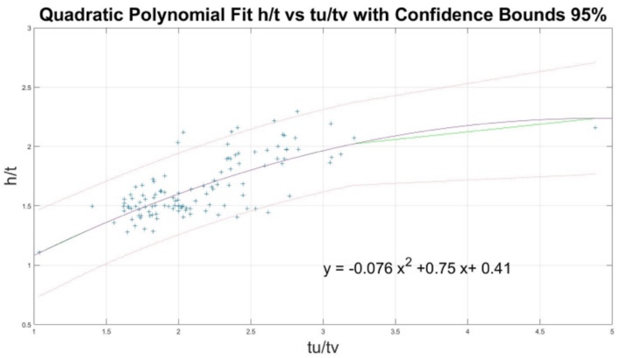


**Figure 15.** Scatterplot of h/t and tu/tv. Squared polynomial fit with a 95 % confidence region.

The relationships found to describe the behavior of the pear shapes as a function of the ring and the tandem residence times are presented in equations 3 and 4 for the linear fit. Equations 5 and 6 represent the quadratic relationship.

$$\frac{h}{w} = 0.301 \times \frac{tu}{tv} + 0.692 \quad (3)$$

$$\frac{h}{t} = 0.355 \times \frac{tu}{tv} + 0.883 \quad (4)$$

$$\frac{h}{w} = -0.043 \times \left(\frac{tu}{tv}\right)^2 + 0.52 \times \frac{tu}{tv} + 0.43 \quad (5)$$

$$\frac{h}{t} = -0.076 \times \left(\frac{tu}{tv}\right)^2 + 0.75 \times \frac{tu}{tv} + 0.41 \quad (6)$$

## 4. Discussion

The dosimetric parameters used in Brachytherapy come from times when procedures were performed with a low dose rate, lacking the contemporary optimization processes.

Using the values of h/w and h/t, it is possible to perform a volumetric reconstruction of the prescription dose, which responds to the geometry of the implant and is determined by the applicators selected according to the patient's anatomy. This reconstruction is superimposed on the target treatment volume, and it is compared with the prescription isodose for coverage.

It is currently possible to carry out optimization processes that achieve the appropriate dose shape in the target volume. This optimization allows variability in the form of the isodose while maintaining the prescribed dose at point A (ICRU 38).

The present work included prescription point A and others arising from the recommendations of ICRU 89 and ABS. These points allow increasing the volumetric resolution, limiting the variations resulting from the optimization processes. In the present study, we sought to determine if there is a correlation between tu/tv with h/w and tu/tv with h/t, as a first approximation to dose shaping. The number of stops during the optimization process was not restricted and the time in each of them obtained a specific shape in the isodoses that comply with the dose prescription at all points (ICRU38, ICRU89, and ABS

Figure 3 shows dwell times at each position for all insertions. It shows on the time axis a box with a line in the center; it represents the median times with the 25th and 75th percentiles indicated by the edges of the box. As can be seen, positions corresponding to the tandem center are the most used in determining the isodose represented by a high range between the percentiles.

Considering the modulation in the tandem zone, our study finds a correlation higher than 0.7 (strong correlation) between tu/tv and h/w in all the groups analyzed (Fig. 4), p-value<0.001, showing that both variables are related even though the source stop times in the insertions were not regulated. In the case of the correlation between tu/tv and h/t (Fig 5), p-value<0.001, the range remained constant between 0.5 and just over 0.7 (Moderate correlation), about 90% of the groups have a correlation value between 0.6 and 0.7, with 4% of groups above 0.7 (Strong correlation). These values could demonstrate that the higher number of prescription points used as a requirement for dose optimization, the more they directly influence the correlation described above.

Likewise, considering the dose differences in the vaginal area, our study finds a strong correlation between the variables tu/tv and h/w for the groups with the higher number of elements and the highest DIF. The correlation gradually decreased until reaching the moderate to low region and rising again for the groups with lower DIF and fewer elements (Fig. 10), p-value <0.001.

In contrast, the correlation between tu/tv and h/t starts moderately for groups with more elements and higher DIF. It decreases non-monotone to a weak correlation for smaller groups and lower DIF (Fig. 11), p-value <0.001 for correlations with groups with more elements and higher DIF, to p-value<0.2 for groups with fewer elements.

The presence of more points in the tandem zone for dose prescription is what we consider the reason why the correlation is strong throughout the range between the variables tu/tv and h/w when M measures precisely the modulation in this zone. However, these same variables are less correlated when M arranges the groups in the vaginal area. Similar is the behavior of the correlation between tu/tv and h/t. The restriction points for dose prescription imposed in the optimization restrict the variability of the pear shape, so this benefits the correlation in the uterine zone. At the same time, in the vaginal site, there is more freedom in the form of the dose volume, as there are fewer prescription points which result in a lower correlation.

In all the figures, a positive relationship between the variables is observed and, in most cases, with a high statistical significance value. The relation between tu/tv with h/w and h/t could be plotted for a linear. Also, the polynomial squared fitting equation with a 95% confidence region for both cases at these 120 sessions (figures 12, 13, 14, and 15). These results led us to identify the possibility of using the tu/tv ratio as a parameter to infer the pear shape in a cervical brachytherapy treat. At the same time, while optimization considers several prescriptions points for the dose.

## 5. Conclusions

Organized for modulation in the uterus using source dwell times, we found a strong correlation between the h/w ratio with tu/tv, greater than 0.7, and a moderate correlation between h/t with tu/tv greater than 0.5. Similarly, taking into account the difference in dwell time between left and right in the vagina, we found a correlation between the ratio h/w with tu/tv from moderate to strong, higher than 0.4, and between h/t with tu/tv from weak, higher than 0.2 to moderate, lower than 0.7. The greater number of prescribed points located around the uterus than in the vaginal region resulted in a higher correlation when groups were ordered by modulation in the uterus, compared to when the correlation was calculated for groups ordered by time difference in the vaginal region.

Fitting tu/tv with h/w and h/t using a polynomial analysis with 95% confidence, we found several possibilities to infer the relationship of the dimensions from the time relationship. The results showed a better fit for h/w and tu/tv than from h/t and tu/tv. In contrast, both cases showed a better fit using a quadratic polynomial equation, but it was significantly better to use this fit for h/t and tu/tv.

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