**UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE**

**PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA REABILITAÇÃO**

**Taís Marques Cerentini**

# Fisioterapia Pélvica em Pacientes Submetidas a Braquiterapia Ginecológica: Ensaio Clínico Randomizado

Porto Alegre

2018

**Taís Marques Cerentini**

# Fisioterapia Pélvica em Pacientes Submetidas a Braquiterapia Ginecológica: Ensaio Clínico Randomizado

Dissertação submetida ao Programa de Pós-Graduação em Ciências da Reabilitação da Fundação Universidade Federal de Ciências da Saúde de Porto Alegre como requisito para a obtenção do grau de Mestre.

Orientador: Prof. Dr. Fabrício Edler Macagnan
Co-orientador: Dra. Patrícia Viana da Rosa

Porto Alegre
2018

Catalogação na Publicação

Cerentini, Taís Marques
Fisioterapia pélvica em pacientes submetidas a braquiterapia ginecológica: Ensaio clínico randomizado / Taís Marques Cerentini. -- 2018.
73 p. : il., graf., tab. ; 30 cm.

Dissertação (mestrado) -- Universidade Federal de Ciências da Saúde de Porto Alegre, Programa de Pós-Graduação em Ciências da Reabilitação, 2018.

Orientador(a): Fabrício Edler Macagnan ; coorientador(a): Patricia Viana da Rosa.

1. Dilatadores Vaginais. 2. Braquiterapia. 3. Câncer do Colo do Útero. 4. Fisioterapia Pélvica. 5. Radioterapia. I. Título.

Sistema de Geração de Ficha Catalográfica da UFCSPA com os dados fornecidos pelo(a) autor(a).

# Fisioterapia Pélvica em Pacientes Submetidas a Braquiterapia Ginecológica: Ensaio Clínico Randomizado

**BANCA AVALIADORA**

_____

Dra. Mirella Dias, Doutora em Ciências Médicas pela Universidade Federal de Santa Catarina - UFSC

Departamento de Fisioterapia

Universidade do Sul de Santa Catarina, UNISUL

_____

Dra. Renata Schvartzman, Doutora em Ciências Médicas pela Universidade Federal do Rio Grande do Sul - UFRGS

_____

Dr. Rodrigo Della Méa Plentz, Pós Doutor pela Fundação Universitária de Cardiologia.

Departamento de Fisioterapia/ Universidade Federal de Ciências da Saúde de

Porto Alegre

Porto Alegre
2018

## DEDICATÓRIA

**Dedico este trabalho à minha família:**

A minha mãe Amélia, de quem tenho muito orgulho e me espelho tanto profissional como pessoalmente, diante de toda sua garra;

Ao meu pai Fernando por me inspirar com seu espírito jovem, amigo, solidário, protetivo e presente;

Ao meu irmão Maicon, por tornar as coisas mais leves e fáceis, pela ajuda, pelo amor e carinho, de quem me orgulho muito.

Ao meu namorado Henrique, por valorizar tudo quanto sou no mínimo que faço, e me incentivar sempre;

**Sem vocês nenhuma conquista valeria a pena!**

Aos meus amigos, que entenderam minhas ausências e me deram incentivo para nunca desistir, em especial a Luana que me deu suporte quando tudo em uma nova cidade parecia novo.

A minha bolsista Júlia Schlöttgen pela imensurável ajuda e incentivo;

Ao meu professor orientador Dr. Fabrício Edler Macagnan, pela oportunidade, confiança, incentivo, paciência, amizade e excelente orientação, sem você este trabalho não seria o mesmo;

A professora Dr. Patrícia Viana da Rosa, que além da co-orientação me presenteou com sua amizade.

**AGRADECIMENTO**

"Cada um que passa na nossa vida passa sozinho, pois cada pessoa é única, e nenhuma substitui outra. Cada um que passa na nossa vida passa sozinho, mas não vai só, nem nos deixa sós. Leva um pouco de nós mesmos, deixa um pouco de si mesmo. Há os que levam muito; mas não há os que não levam nada. Há os que deixam muito; mas não há os que não deixam nada. Esta é a maior responsabilidade de nossa vida e a prova evidente que duas almas não se encontram ao acaso."

Saint-Exupéry

Para concretizar este trabalho, contei com a disponibilidade, apoio e colaboração de muitas pessoas. Para elas o meu reconhecimento.

Manifesto a minha gratidão ao Prof. Dr. Fabrício E. Macagnan, orientador desta tese, pela oportunidade dada a mim e por acreditar que eu era capaz de realizar este trabalho. Obrigada pelas críticas e conselhos, mas, sobretudo pelo estímulo e ajuda na concretização deste projeto.

Agradeço a Prof. Dr. Patrícia Viana da Rosa pela confiança e todas as aprendizagens e experiências que me permitiu vivenciar, além da amizade que estimo.

A Ms. Karoline C. Bragante pelo auxílio nas dúvidas durante a condução deste estudo.

A minha bolsista Júlia Schlöttgen que me auxiliou durante as coletas e foi indispensável para que tudo desse certo. Também a Thayná Silva pela ajuda durante as coletas

Agradeço a toda equipe da radioterapia do Hospital Santa Rita da Santa Casa de Misericórdia de Porto Alegre. A equipe médica por apostar neste trabalho e esclarecer minhas dúvidas e a equipe de enfermagem e técnicos de enfermagem que foram incansáveis na ajuda com as coletas. O incentivo e colaboração de vocês foi imensurável na condução deste trabalho.

A Cristiane Bündchen em nome do NUPESC pela impagável ajuda com a estatística e por toda a paciência ao me auxiliar deste trabalho;

Aos membros da banca examinadora, Dra. Mirella Dias, Dra. Renata Schvartzman, e Dr. Rodrigo Della Méa Plentz, que gentilmente aceitaram participar e colaborar com esta dissertação;

Aos meus amigos queridos, Caroline, Dilene, Francine, Thamiris, Isnara, Elder, Rafael, Daniel, Giovani, Alan e Bruno.

A equipe do Hospital Fêmina que se tornaram grandes amigas, Leila, Jordana e Patrícia.

A minhas pacientes, mulheres com as quais o conhecimento foi muito além da clínica. Sem elas este trabalho não seria possível.

## RESUMO

**Introdução:** O câncer do colo do útero é a neoplasia ginecológica mais comum no mundo, configurando a quarta causa de morte das mulheres no Brasil. A braquiterapia ginecológica é um tratamento adjuvante que auxilia na remissão neoplásica promovendo aumento da sobrevida. Entretanto, a irradiação ionizante afeta negativamente o canal vaginal, podendo causar além de outras desordens, alterações nas dimensões do canal vaginal associada à morbidade mais prevalente após o tratamento com altas doses de radiação. **Objetivo:** Avaliar as dimensões do canal vaginal nas pacientes submetidas à braquiterapia ginecológica e o efeito do uso de dilatadores vaginais (DV) empregados no acompanhamento de fisioterapia pélvica. **Métodos:** Este estudo é um ensaio clínico randomizado, no qual 88 participantes foram alocadas randomicamente nos grupos controle (GC: n = 32) e intervenção (GI: n = 56). Foram realizadas três avaliações: pré-braquiterapia, pós-braquiterapia e no follow up de 3 meses. O GC recebeu orientações habituais da equipe de saúde, enquanto que o GI foi orientado à utilizar DV durante três meses. As dimensões do canal vaginal (desfecho principal) foram definidas pelo comprimento da vagina (cm), largura (número de voltas horárias da rosca de abertura no espéculo ginecológico) e área (definida através do tamanho do DV). Foram avaliadas também a qualidade de vida (QV) e a funcionalidade do assoalho pélvico (AP). **Resultados:** Não houve efeito do DV sobre o comprimento vaginal (p = 0,111), largura (p = 0,490) e área (p = 0,743). Na análise estratificada por adesão, o GC teve significativa diminuição da área vaginal (p = 0,046). O AP foi predominantemente hipoativo (GC: 59,4%; GI: 69,9%) ao longo do seguimento. A QV melhorou em ambos os grupos, mas a redução de constipação, ressecamento vaginal e incontinência urinária de esforço se manifestou apenas no GI. **Conclusão***:* O uso de DV não alterou as dimensões do canal vaginal nos primeiros três meses após o término do tratamento de RT para o câncer do colo uterino. Porém, houve grande perda amostral ao longo do seguimento e por isso, estudos com maior número amostral e tempo de

seguimento precisam ser conduzidos para avaliar o benefício do DV sobre as dimensões vaginais, funcionalidade do AP e evolução clínica.

**Palavras-chave:** Radioterapia; Dilatadores Vaginais; Câncer do Colo do Útero; Fisioterapia Pélvica, Braquiterapia

## ABSTRACT

**Introduction:** Cervical cancer is the most common gynecological neoplasia in the world, making it the fourth leading cause of death for women in Brazil. Gynecological brachytherapy is an adjuvant treatment that assists in neoplastic remission promoting increased survival. However, ionizing irradiation negatively affects the vaginal canal and may cause, in addition to other disorders, alterations in the dimensions of the vaginal canal, associated with the most prevalent morbidity after treatment with high doses of radiation. **Objective**: To evaluate the dimensions of the vaginal canal in patients undergoing gynecological brachytherapy and the effect of the use of vaginal dilators (VD) used in the follow-up of pelvic physiotherapy. **Methods:** This is a randomized clinical trial in which 88 patients were allocated randomly in the control (CG: n = 32) and intervention (IG: n = 56) groups. Three evaluations were performed: pre-brachytherapy, post-brachytherapy and follow-up of 3 months. The CG received standard guidance from the health team while IG was instructed to use VD for three months. The dimensions of the vaginal canal (main outcome) were defined by the length of the vagina (cm), width (number of full clockwise turns of the opening thread in the gynecological speculum) and area (defined by the size of the VD). Quality of life (QOL) and pelvic floor (PF) functionality were also evaluated. **Results:** There was no effect of the VD on vaginal length ($p = 0.111$), width ($p = 0.490$) and area ($p = 0.743$). In the analysis stratified by adhesion, the CG had a significant decrease in the vaginal area ($p = 0.046$). PF was predominantly hypoactive (CG: 59.4%, IG: 69.9%) throughout the follow-up. QoL improved in both groups, but the reduction of constipation, vaginal dryness, and stress urinary incontinence manifested only in IG. **Conclusion:** The use of VD did not alter the dimensions of the vaginal canal within the first three months after the end of RT treatment for cervical cancer. However, there was a large sample loss during follow-up and therefore, studies with a larger sample number and longer follow-up time need to be conducted to evaluate the benefit of VD on vaginal dimensions, PF functionality and clinical evolution.

**Keywords:** Radiotherapy; Vaginal Dilators; Cervical Cancer; Pelvic Physiotherapy; Brachytherapy

## LISTA DE FIGURAS

**Referencial teórico:**



**Artigo:**

## LISTA DE TABELAS

## LISTA DE ABREVIATURAS E SIGLAS

| | |
|---|---|
| **Gy** | Greys |
| **RT** | Radioterapia |
| **HPV** | Papilomavirus humano |
| **GC/CG** | Grupo controle |
| **GI/IG** | Grupo intervenção |
| **DV/VD** | Dilatadores vaginais |
| **TCLE** | Termo de Consentimento Livre e Esclarecido |
| **EORTC QLQ-C30** | Questionário de qualidade de vida European Organization for Research and Treatment of Cancer |
| **GEE** | Método estatístico de Modelo de Equações de Estimativas Generalizadas |
| **ITT** | Método estatístico de Intenção de Tratar |
| **SPSS** | Software de análises estatísticas IBM SPSS |
| **DCF-AP/ KFD-PF** | Diagnóstico Cinesiológico Funcional do Assoalho Pélvico |
| **QV/ QL** | Qualidade de Vida |
| **AP/PF** | Assoalho Pélvico |

**SUMÁRIO**

## 1 INTRODUÇÃO

Câncer é a denominação dada ao tumor maligno, no qual ocorre crescimento celular anormal (SOARES; SILVA, 2010), de etiologia multivariada que configura um problema de saúde pública (TAVARES; PRADO, 2006). As estimativas no Brasil para a incidência de câncer no biênio 2018/2019 é de 600 mil novos casos para cada ano (INSTITUTO NACIONAL DE CâNCER JOSÉ ALENCAR GOMES DA, 2018).

O câncer ginecológico inclui o câncer de cérvix uterino, de corpo uterino, de ovário, de vulva e vagina, sendo a terceira causa de morte mais comum de mulheres nos Estados Unidos (FAUBION et al., 2015a). O câncer do colo do útero é uma preocupação global e a neoplasia ginecológica mais comum no mundo configurando a quarta causa de morte das mulheres no Brasil, estimando-se 16.370 novos casos para cada ano do biênio 2018/2019, seguido pelo câncer de endométrio e de ovário (OLIVEIRA et al., 2010; MAHMUD et al., 2011; INSTITUTO NACIONAL DE CÂNCER JOSÉ ALENCAR GOMES DA, 2018).

A braquiterapia ginecológica é frequentemente utilizada nestes casos, visando a remissão da doença e melhorando a taxa de sobrevivência das pacientes (ZOMKOWSKI et al., 2016), porém a mucosa vaginal é exposta a altas e médias doses de radiação, o que pode acarretar em efeitos a médio e longo prazo como a estenose vaginal, telangiectasias, dispareunia, secura vaginal, palidez vaginal, dentre outros (THOMAS et al., 1998; MOHAMED et al., 2016).

Alterações nas dimensões do canal vaginal podem ocorrer nas mulheres que recebem este tipo de tratamento (HOFSJÖ et al., 2017) e sua diminuição afeta negativamente a qualidade de vida, a função sexual podendo interferir em exames físicos (MILES; JOHNSON, 2014; PARK et al., 2015).

Visto que a radiação leva a perda da elasticidade, endurecimento, rigidez, retração e ulceração, mudanças associadas a hiperpigmentação, epilação, ressecamento da pele e telangiectasias em outros tecidos (DELANIAN; LEFAIX, 2004), na mucosa vaginal, tecidos conjuntivos e pequenos vasos sanguíneos não seria diferente. Há o desenvolvimento de telangiectasias, hialinização do tecido conjuntivo vaginal e fibrose nas fibras musculares. Ocorre posterior atrofia que

conduz ao estreitamento e perda da lubrificação, formação de aderências e fibroses com consequente perda da elasticidade vaginal (LANCASTER, 2004; PARK et al., 2015; KIRCHHEINER et al., 2016).

Os métodos avaliativos das dimensões do canal vaginal são bastante controversos, não havendo um consenso nem padronização entre autores (SOARES; SILVA, 2010). Para manter a funcionalidade do canal vaginal, o tratamento indicado é o uso regular de dilatadores vaginais e, a prática de relações sexuais de duas a três vezes por semana, visando manter a permeabilidade vaginal (PARK et al., 2015). Em revisão sistemática, Miles e Johnson (2014) enfatizam a importância de uma terapia que minimize os danos da radiação, pois além de manter a vagina patente (aberta) para as relações sexuais, permite o exame ginecológico para acompanhar se houver a recorrência do câncer.

Diante disso, o objetivo deste estudo foi avaliar o efeito do uso dos dilatadores vaginais sobre as dimensões do canal vaginal de pacientes submetidos à braquiterapia ginecológica.

# 2 REVISÃO DE LITERATURA - CONTEXTUALIZAÇÃO

## 2.1 câncer

Câncer é a denominação dada a todo tumor maligno no qual ocorre um crescimento celular anormal decorrente da perda do controle biológico intrínseco (SOARES; SILVA, 2010), sendo um processo comum, heterogêneo, de etiologia multivariada, diferentes sintomas clínicos e prognóstico, levando ao aumento progressivo de sua incidência (TAVARES; PRADO, 2006).

Segundo o *World Câncer Report* 2014, é a maior causa de morbidade e mortalidade, afetando as populações de todas regiões do mundo, sendo considerado um problema de saúde pública, característico de países em desenvolvimento, prevendo mais de 20 milhões de novos casos para 2025 (STEWART; WILD, 2014). Determinados tipos de câncer são observados em países desenvolvidos como o de próstata, mama e intestino e outros mais em países subdesenvolvidos, relacionados às condições socioeconômicas da população como o câncer do colo do útero e do estômago. Com base nisto, é fundamental monitorar a morbimortalidade do câncer por rotina e estabelecer ações de prevenção e controle do câncer e seus fatores de risco (INSTITUTO NACIONAL DE CÂNCER JOSÉ ALENCAR GOMES DA, 2018).

Apesar do organismo humano estar exposto a diversos agentes carcinogênicos, a predisposição individual é de suma importância no desenvolvimento ou não de uma resposta a esta exposição. As células sofrem mutação espontânea e alteram seu desenvolvimento normal, isto inclui danos oxidativos, erros de ação de polimerases e das recombinases e redução e reordenamento cromossômico. Ou seja, a carcinogênese pode iniciar espontaneamente ou em reação a agentes químicos, físicos ou biológicos (INSTITUTO NACIONAL DE CÂNCER JOSÉ ALENCAR GOMES DA SILVA, 2016). A incidência, distribuição geográfica e comportamento das neoplasias depende de fatores como sexo, idade, raça, predisposição genética, e exposição a agente carcinogênicos, podendo levar muitos anos para que a carcinogênese

se complete e o tumor apareça (INSTITUTO NACIONAL DE CâNCER JOSÉ ALENCAR GOMES DA, 2018).

Figura 1 – Distribuição proporcional dos dez tipos de câncer mais incidentes estimados para 2018 por sexo, exceto pele não melanoma

| Localização Primária | Casos | % | | | Localização Primária | Casos | % |
|---|---|---|---|---|---|---|---|
| Próstata | 68.220 | 31,7% | Homens | Mulheres | Mama Feminina | 59.700 | 29,5% |
| Traqueia, Brônquio e Pulmão | 18.740 | 8,7% | | | Cólon e Reto | 18.980 | 9,4% |
| Cólon e Reto | 17.380 | 8,1% | | | Colo do Útero | 16.370 | 8,1% |
| Estômago | 13.540 | 6,3% | | | Traqueia, Brônquio e Pulmão | 12.530 | 6,2% |
| Cavidade Oral | 11.200 | 5,2% | | | Glândula Tireoide | 8.040 | 4,0% |
| Esôfago | 8.240 | 3,8% | | | Estômago | 7.750 | 3,8% |
| Bexiga | 6.690 | 3,1% | | | Corpo do Útero | 6.600 | 3,3% |
| Laringe | 6.390 | 3,0% | | | Ovário | 6.150 | 3,0% |
| Leucemias | 5.940 | 2,8% | | | Sistema Nervoso Central | 5.510 | 2,7% |
| Sistema Nervoso Central | 5.810 | 2,7% | | | Leucemias | 4.860 | 2,4% |

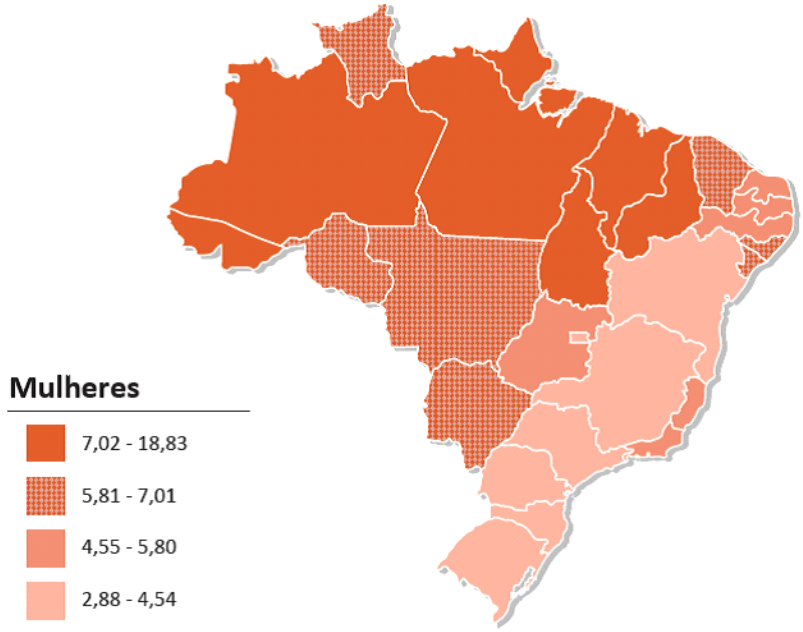
Fonte: http://www.inca.gov.br/estimativa/2018/

O câncer ginecológico inclui o câncer do colo do útero, de corpo uterino, de ovário, de vulva e de vagina, sendo a terceira causa de morte mais comum de mulheres nos Estados Unidos, tendo como fatores de risco agentes comportamentais, reprodutivos e hormonais (FAUBION et al., 2015b; HUANG et al., 2016).

Em países desenvolvidos os tipos de câncer ginecológicos que mais ocorrem são corpo uterino e ovário, e estão associados a fatores como obesidade, diminuição do número de filhos e exposições a estrogênios. O câncer do corpo do útero constitui o sexto câncer mais comum na população feminina, com uma estimativa de 6.600 casos novos para cada ano do biênio 2018-2019 (INSTITUTO NACIONAL DE CÂNCER JOSÉ ALENCAR GOMES DA, 2018). Em países subdesenvolvidos o câncer mais comum é a neoplasia cervical, que ocorre em 50% a 70% por infecção com papilomavírus humano (HPV) (HUANG et al., 2016; OLSON et al., 2016), configurando a quarta causa de morte por câncer em mulheres no Brasil e o terceiro tumor mais frequente na população feminina, atrás do câncer de mama e do colorretal, estimando-se 16.370 novos casos para cada ano do biênio 2018-2019, com um risco estimado de 15,43 casos a cada 100 mil

mulheres (INSTITUTO NACIONAL DE CâNCER JOSÉ ALENCAR GOMES DA, 2018).

Figura 2 – Representação espacial das taxas ajustadas* de incidência por 100 mil mulheres, estimadas para o ano de 2018 segundo Unidade da Federação (neoplasia maligna do colo do útero)




Fonte: http://www.inca.gov.br/estimativa/2018/

### 2.1.1 Câncer do colo do útero

O câncer do colo de útero, também conhecido como câncer cervical leva a uma alteração do revestimento do colo do útero (PHILLIPS et al., 2016), decorrente da replicação desordenada deste epitélio, o que compromete o estroma e pode difundir-se para estruturas e órgãos proximais ou distantes. (INSTITUTO NACIONAL DO CÂNCER JOSÉ DE ALENCAR, 2000).

O tipo histológico mais comum do câncer do colo do útero é o carcinoma de células escamosas que acomete o epitélio escamoso e representa cerca de 85% a 90% dos casos, seguido pelo adenocarcinoma, mais raro e que acomete o epitélio glandular (INSTITUTO NACIONAL DO CÂNCER JOSÉ DE ALENCAR, 2000). Há diversos fatores envolvidos na etiologia do câncer do colo do útero, mas

as infecções persistentes pelo HPV é o principal deles (INSTITUTO NACIONAL DE CÂNCER JOSÉ ALENCAR GOMES DA, 2018). Sabe-se que existem 40 genomas do Papilomavirus humano (HPV) mapeados, e que a infecção e persistência do mesmo é necessária para que o câncer do colo do útero se desenvolva, sendo os tipos 16 e 18 considerados de alto risco para o desenvolvimento da neoplasia, presentes em 70% dos casos (INSTITUTO NACIONAL DO CÂNCER JOSÉ DE ALENCAR, 2000).

Existem métodos preventivos para rastrear o câncer do colo do útero, sendo o mais comum o teste citológico realizado durante o exame pélvico, através do qual se obtém uma amostra de células do colo do útero, visando identificar lesões que tem potencial para se tornarem cancerígenas (OLSON et al., 2016). Realização de teste citológico em larga escala, teste para HPV e vacinação para HPV podem reduzir os índices de câncer de colo de útero e sua mortalidade (PETRY; PETRY, 2014). Além do HPV, fatores como imunidade, genética, comportamento sexual, multiparidade, tabagismo e uso prolongado de estrogênio podem influenciar no mecanismo da doença (STEWART; WILD, 2014).

No Brasil, o Ministério da Saúde possui diretrizes para o rastreamento do câncer do colo do útero, no qual recomenda a citopatologia em mulheres de 25 a 64 anos a cada três anos, após dois exames anuais consecutivos com resultados normais. Em lesões de baixo grau, recomenda-se o acompanhamento de seis em seis meses. O câncer do colo uterino possui alto potencial de cura quando diagnosticado em estágios iniciais (MINISTÉRIO DA SAÚDE, 2016).

## 2.2 Tratamento

Os métodos para tratamento dos tumores ginecológicos são a cirurgia, a radioterapia (RT) e a quimioterapia e sua escolha irá depender do estádio da doença (SILVA et al., 2010), sendo a terapia por radiação amplamente utilizada para seu tratamento (HATA et al., 2013).

As pacientes com neoplasia do colo do útero utilizam radioterapia, nas formas externa ou intracavitária (RAKHRA et al., 2016) visando o impedimento da

reprodução do ácido desoxirribonucleico (DNA) das células, induzindo à apoptose, e apesar de danificar também as celular normais, estas conseguem reparar-se com maior eficiência (FRIGATO, S. HOGA, 2003). Quando há indicação de investigação da junção endocervical, pode ser indicada a realização de uma conização e/ou seguimento do acompanhamento (MINISTÉRIO DA SAÚDE, 2016).

### 2.2.1 Conização

É a retirada de uma porção significativa do canal endocervical nos colos em que não é possível ter a visão através da colposcopia no interior do canal. Indicada com objetivo diagnóstico quando há necessidade de avaliação do canal endocervical e já se realizou o escovado endocervical para exame citopatológico, entretanto, se ao examinar o canal endocervical for possível ver a junção escamocolunar, esse procedimento pode ser evitado ou adaptado a profundidade do cone à extensão da lesão dentro do canal (MINISTÉRIO DA SAÚDE, 2016). Quando realizada a retirada de um cone do colo uterino faz-se o exame anatomopatológico da peça operatória, que irá classificar o grau de lesão e o seu nível de invasão (INSTITUTO NACIONAL DO CÂNCER JOSÉ DE ALENCAR, 2000).

É utilizada para tratamento quando não houver invasão ou a mulher apresentar NIC II/III, sendo considerada um tratamento suficiente, desde que assegurada um acompanhamento rigoroso (MINISTÉRIO DA SAÚDE, 2016). Em lesões primárias de alto grau, a conização é preconizada, e pode ser realizada pelas técnicas tradicional (bisturi a frio), a laser e por cirurgia de alta frequência (CAF) (SIMÕES, 2012).

Segundo Simões (2012) a conização a frio é indicada quando há atrofia cervical, diagnostico de lesão glandular e suspeita de invasão estromal, por apresentar maior risco de complicações e comprometer a reprodutividade das pacientes. O procedimento a laser tem custo elevado e exige maior treinamento do cirurgião, por este motivo nem sempre seu uso é empregado.

### 2.2.2 Teleterapia

Quando se realiza a radioterapia na pelve feminina, alguns locais são de difícil proteção, como as alças intestinais, medula óssea hematopoiética pélvica, reto, bexiga e articulações coxofemorais, sendo as doses indicadas para tratar os tumores maiores do que as toleradas por estas estruturas, o que pode comprometer a qualidade de vida destas pacientes. Devido este fato, a modulação do feixe de radioterapia é altamente indicado no caso de tumores ginecológicos (CONJUNTO et al., 2013). A radiação diminui os índices de recidivas, pode ser associada à quimioterapia e complementar a técnica cirúrgica. É determinado um alvo para a radiação e os tecidos periféricos sofrem menos em decorrência da mesma, pois há menos chances de os mesmos serem afetados (FRIGATO, S. HOGA, 2003).

A teleterapia, também conhecida como radiação externa, faz uma distribuição de dose razoável sobre o tumor, porém as demais estruturas adjacentes não ficam livres de receber esta radiação (RAM ABHINAV et al., 2013). O feixe de radiação é apontado para a região alvo a uma distância de 60 a 100 cm do paciente, através de um acelerador linear (SILVA et al., 2010) e normalmente se utiliza fontes de origem nuclear, que produzem a radiação por meio da aceleração de elétrons. A dose total neste tipo de radiação é fracionada em aplicações diárias, que são subdivididas em um campo anterior, um posterior e dois laterais para realizar-se a radiação pélvica (FRIGATO, S. HOGA, 2003).

### 2.2.3 Braquiterapia

A aplicação de radiação diretamente no tumor, através do contato direto ou muito próximo a ele é chamada de braquiterapia, técnica que permite a radiação direta no tecido tumoral e menor contato com outros tecidos, sendo amplamente utilizada nos cânceres ginecológicos (LANCASTER, 2004). Sua finalidade é não afetar estruturas vizinhas ao tumor, através da implantação de moldes, cateteres ou aplicadores que permitem a radiação localizada e normalmente é utilizada como um complemento da radioterapia externa (FRIGATO, S. HOGA, 2003).

Pode ser ofertada em baixa e alta dose (LANCASTER, 2004). A braquiterapia de baixa dose requer um período de tempo de radiação mais longo (aproximadamente 24-96 horas), sendo um tratamento contínuo que demanda internação hospitalar (FRIGATO, S. HOGA, 2003). Já a braquiterapia de alta dose requer um menor período de exposição à radiação (geralmente menos de 10 minutos), sem necessidade de internação (LANCASTER, 2004).

### 2.3 Efeitos adversos da radioterapia

Os efeitos adversos induzidos pela radioterapia têm causa multifatorial (DUNBERGER et al., 2011). A toxicidade aos tecidos depende da radiossensibilidade e tolerância ao esquema terapêutico empregado, o que afeta tanto as células tumorais quanto as células saudáveis. Outros fatores que podem interferir no surgimento de efeitos secundários à radioterapia são o volume do tumor, a dose de radiação administrada e a condição clínica do paciente. Alguns fatores como irritabilidade vesical, diarreia, alterações cutâneas, fístulas intestinais ou vesicais e fibrose vaginal podem ser inevitáveis ao tratamento (ROSA et al., 2016).

Fibrose é um processo dinâmico, que se caracteriza pela remodelação constante e ativação de fibroblastos ao longo do tempo. Imediatamente após receber a radiação, uma cascata de ativação de citocinas é iniciada e pode persistir por longos períodos de tempo, desenvolvendo consequências tardias (MARTIN; LEFAIX; DELANIAN, 2000).

O TGF-β1 é a isoforma mais aplicada em doenças fibroproliferativas e quando está alterado resulta em modificações na sua proliferação e apoptose, sendo considerado a provável citocina mais responsável pela reação fibrótica nos tecidos expostos a radiação (RODEMANN; BAMBERG, 1995; MARTIN; LEFAIX; DELANIAN, 2000).

A indução de TGF-β1 inicia aproximadamente seis horas após a exposição de 16 a 64 Gy e sua produção anormal em tecidos irradiados resulta na expressão contínua de sinais de reparação tecidual e células de ativação. Em tecidos superficiais, se caracteriza pelo endurecimento da derme e tecido subcutâneo,

que está associado a telangiectasias e hialinização do colágeno da derme reticular. Já a epiderme pode torna-se hiperplástica ou atrófica (MARTIN; LEFAIX; DELANIAN, 2000).

Em revisão sobre o processo de fibroatrofia radio-induzida, Delanian e Lefaix (2004) mencionam que superficialmente podem ocorrer mudanças cutâneo musculares como: perda da elasticidade, endurecimento, rigidez, retração e ulceração, mudanças associadas a hiperpigmentação, epilação, ressecamento da pele e telangiectasias.

A fibroatrofia ocorre gradualmente e vai se agravando ao longo dos anos com consequente lesão irreversível. Este processo é dividido na fase pré-fibrótica que são os primeiros meses após a radioterapia, normalmente assintomática, entretanto pode apresentar marcadores específicos de resposta inflamatória local; a fase construtiva que ocorre nos primeiros anos após a radioterapia e consiste na organização da fibrose e desaparecimento dos marcadores de resposta inflamatória e o aparecimento de tecido grosso e endurecido com capilares alargados; e a fase de fibroatrofia tardia, na qual há atrofia retrátil e destruição gradual concomitante dos tecidos normais que ocorre de 5 a 30 anos após a radioterapia (DELANIAN; LEFAIX, 2004).

### 2.3.1 Efeitos locais da radiação ionizante

A radiação causa danos à mucosa vaginal, tecidos conjuntivos e pequenos vasos sanguíneos com consequente desnudamento do epitélio vaginal e aporte reduzido de sangue que acarreta em hipóxia dos tecidos vaginais e desenvolvimento de telangiectasias. Ocorre a hialinização do tecido conjuntivo vaginal e fibrose nas fibras musculares. Posteriormente ocorre a atrofia que conduz ao estreitamento e perda da lubrificação enquanto que o processo cicatricial, a formação de aderências e a fibrose levam a perda da elasticidade vaginal. Se não houver um processo preventivo, essa cascata de eventos pode levar à obliteração completa da vagina (LANCASTER, 2004; PARK et al., 2015; MOHAMED et al., 2016).

Esta perda do epitélio vaginal ocorre durante os primeiros 3 a 6 meses após a radiação, e a reepitelização que ocorre deixa a superfície com uma camada fina e incompleta de células (WOLF, 2006). Algumas mudanças estruturais que ocorrem em outros locais, como bexiga e intestino são bem estabelecidas, entretanto são poucos os estudos que analisaram as mudanças morfológicas do canal vaginal decorrente da radiação. A palidez da mucosa vaginal pode ser causada pela atrofia do epitélio e possível hipovascularização e hipóxia (HOFSJÖ et al., 2017).

Outro fator que pode desencadear a perda da elasticidade, lubrificação, adelgaçamento e atrofia da vagina é a deficiência estrogênica, em função da perda ou diminuição da função dos ovários (LANCASTER, 2004; PARK et al., 2015; MOHAMED et al., 2016). Entretanto, diferente do período de pós-menopausa no qual a deficiência estrogênica pode ser corrigida pelo uso tópico da mesma, sugere-se que as mudanças vaginais radio-induzidas tornam a vagina menos responsiva, tanto ao estrogênio tópico como sistêmico, acreditando-se que a radiação leva a uma alteração na função dos receptores de estrogênio (HOFSJÖ et al., 2017).

Em estudo recente em sobreviventes de câncer de colo uterino Hofsjö e colaboradores (2017) encontraram fibrose e elastose no tecido conectivo, com alta densidade de colágeno e numeroso emaranhado de fibras elásticas nas paredes vaginais. Segundo os autores, essa mudança morfológica acompanhou a dose recebida, ou seja, quanto maior a dose, maior a mudança. Porém, quando observaram microscopicamente o tecido da vagina, viram que a fibras elásticas estavam distribuídas de forma disfuncional, o que explicaria os sintomas relatados pelas pacientes como, inelasticidade e estreitamento vaginal, com consequente dispareunia e rigidez de tecidos durante o exame ginecológico.

A dor relatada pelas pacientes provavelmente decorre da atrofia do epitélio e possível hipovascularização e hipóxia. O tratamento resulta em baixos níveis de estrogênio circulante devido a possível alteração na função dos receptores de estrogênio tópico e sistêmico causada pela radiação. Os autores sugerem que o

uso precoce de dilatador vaginal e estrogênio pode preservar a funcionalidade vaginal (HOFSJÖ et al., 2017).

## 2.4 Fisioterapia pélvica em oncologia

As terapias utilizadas no tratamento do CA ginecológico podem causar consequências negativas sobre a função do assoalho pélvico (RUTLEDGE et al., 2010), como incontinência urinária, fecal e disfunções sexuais (JOO et al., 2012). A fisioterapia pélvica em oncologia tem como objetivo manter a funcionalidade do canal vaginal e prevenir e/ou tratar os efeitos adversos da radioterapia. Para que isso seja possível é necessária uma avaliação minuciosa do canal vaginal, buscando possíveis alterações funcionais que mais tarde afetarão a qualidade de vida da mulher.

Na literatura muito se utiliza o termo estenose vaginal, que é definida como estreitamento e encurtamento do canal vaginal, que ocorre tardiamente (MOHAMED et al., 2016). Entretanto, poucos são os estudos que avaliam a largura vaginal, considerando apenas o comprimento para classificar essas alterações como estenose (POLAT et al., 2016). Ainda assim, não há um consenso de como deve ser realizada a avaliação para o correto acompanhamento das medidas do canal vaginal, a fim de acompanhar o desenvolvimento de estreitamentos (WOLF, 2006; SILVA et al., 2010). Para avaliar o comprimento vaginal, normalmente utiliza-se um histerômetro, posicionando do anel himenal até o fórnice posterior da vagina, obtendo-se assim o comprimento do canal (POLAT et al., 2016).

Vários métodos são descritos para avaliar a estenose vaginal, porém há uma ausência de padronização e inconsistência em relação à variabilidade de rigores metodológicos (SILVA et al., 2010). Alguns autores consideram alteração quando há diminuição do comprimento da vaginal menor que 8cm (FLAY; MATTHEWS, 1995), a 9 cm (BAHNG et al., 2012). Outros, classificam a estenose em graus (BRAND; BULL; CAKIR, 2006; SILVA et al., 2010). Há também avaliação da mucosa vaginal classificando como normal, parcialmente modificado ou gravemente modificado (SILVA et al., 2010). Kirchheiner e colaboradores

(2016) também utilizam a introdução do espéculo ginecológico de número um para definir a presença ou não de estenose. Porém os métodos de avaliação ainda são muito inconsistentes e há grande variabilidade no rigor de pesquisas em diferentes estudos (DENTON; MAHER, 2003).

Atualmente, vários estudos tem utilizado o *Common Terminology Criteria for Adverse Events* (CTCAE) *Version* 4.0 - 2009*, Version* 4.03 – (2010), publicado pelo *National Cancer Institute* para classificar a estenose vaginal em graus, de acordo com a funcionalidade do canal vaginal em: Grau 1: assintomática, leve encurtamento ou estreitamento vaginal; Grau 2: estreitamento vaginal e/ou encurtando não interferindo com a realização do exame físico; Grau 3: estreitamento vaginal e/ou encurtamento que interfere no uso de tampões, atividade sexual ou exame; Grau 4: não há determinação; Grau 5: morte (NATIONAL INSTITUTE OF CANCER, 2010).

Visando manter a funcionalidade e prevenir as alterações das dimensões do canal vaginal o dilatador vaginal é amplamente indicado para mulheres que realizam radioterapia pélvica, sendo prática comum em vários países (MILES; JOHNSON, 2014; BAKKER et al., 2015). Ele é um dispositivo liso e cilíndrico que tem por objetivo separar mecanicamente as paredes vaginais e esticar os tecidos (CULLEN et al., 2013). A indicação de utilização dos dilatadores varia de três vezes por semana até um tempo indefinido, durante a radioterapia, após ela, ou assim que for confortavelmente possível (MILES; JOHNSON, 2014).

A dilatação vaginal regular pode minimizar os efeitos colaterais da braquiterapia ginecológica como a estenose, cicatrizes e dor, além de possibilitar a capacidade da paciente tolerar a inserção do espéculo para exames ginecológicos (CULLEN et al., 2013).

Cullen e colaboradores (2012) enfatizam que o uso dos DV acaba por ser uma terapia limitada, devido à falta de adesão das mulheres ao seu uso a longo prazo que pode estar atribuído a fatores como ansiedade, modéstia, dor após o uso ou medo de sentir a dor, medo de danificar a vagina, sensação de falta de habilidade de colocar um objeto dentro da vagina e informações insuficientes

sobre o uso do dilatador (CULLEN et al., 2013) o que enfatiza a necessidade de se fornecer informação e apoio a estas mulheres (BRAND; DO; STENLAKE, 2012).

## 3 OBJETIVOS

### 3.1 Objetivo Geral

Avaliar as dimensões do canal vaginal nas pacientes submetidas à braquiterapia ginecológica e o efeito do uso de dilatadores vaginais empregados no acompanhamento de fisioterapia pélvica.

### 3.2 Objetivos Específicos

- Avaliar as diferentes dimensões do canal vaginal
    - Comprimento
    - Largura
    - Área
- Avaliar a funcionalidade da musculatura do assoalho pélvico;
- Evolução clínica dos sinais e sintomas do tratamento de câncer do colo uterino;
- Avaliar a qualidade de vida

## 4 REFERÊNCIAS DA REVISÃO DE LITERATURA


BAHNG, A. Y.; DAGAN, A.; BRUNER, D. W.; LIN, L. L. Determination of prognostic factors for vaginal mucosal toxicity associated with intravaginal high-dose rate brachytherapy in patients with endometrial cancer. **International Journal of Radiation Oncology Biology Physics**, v. 82, n. 2, p. 667–673, 2012.

BAKKER, R. M.; VERMEER, W. M.; CREUTZBERG, C. L.; MENS, J. W. M.; NOUT, R. A.; TER KUILE, M. M. Qualitative accounts of patients' determinants of vaginal dilator use after pelvic radiotherapy. **Journal of Sexual Medicine**, v. 12, n. 3, p. 764–773, 2015.

BRAND, A. H.; BULL, C. A.; CAKIR, B. Vaginal stenosis in patients treated with radiotherapy for carcinoma of the cervix. **International Journal of Gynecological Cancer**, v. 16, n. 1, p. 288–293, 2006.

BRAND, A. H.; DO, V.; STENLAKE, A. Can an educational intervention improve compliance with vaginal dilator use in patients treated with radiation for a gynecological malignancy? **International Journal of Gynecological Cancer**, v. 22, n. 5, p. 897–904, 2012.

BRUNER, D. W. *et al.* Measurement of vaginal length: reliability of the vaginal sound – a Gynecologic Oncologyc Group Study. **International Journal Gynecological Cancer,** v. 16, n. 2, 1749–1755, 2006.

COLOMBO, N. *et al.* **Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.** Annals of Oncology, n..23, Supplement 7, vii27–vii32, 2012.

Common Terminology Criteria for Adverse Events (CTCAE). V4.03: June 14, 2010. U.S.Department of Health and Human Services.

CONJUNTO, E. M.; ASSOCIAÇÃO, C. O. M. a; BRASILEIRA, M.; PROVA, D. D. a; LOCAL, H. E.; PAULO, S. Sociedade Brasileira de Radioterapia – SBRT Sociedade Brasileira de Radioterapia – SBRT. n. 55, p. 1–11, 2013.

CULLEN, K.; FERGUS, K.; DASGUPTA, T.; KONG, I.; FITCH, M.; DOYLE, C.; ADAMS, L. Toward clinical care guidelines for supporting rehabilitative vaginal dilator use with women recovering from cervical cancer. **Supportive Care in Cancer**, v. 21, n. 7, p. 1911–1917, 2013.

DELANIAN, S.; LEFAIX, J. The radiation-induced fibroatrophic process : therapeutic perspective via the antioxidant pathway. **Radiother Oncology**, v. 73, p. 119–131, 2004.

DENTON, A. S.; MAHER, E. J. Interventions for the physical aspects of sexual dysfunction in women following pelvic radiotherapy. **Cochrane Database of Systematic Reviews**, n. 1, p. CD003750, 2003.

DISCROLL, S. D. LYNN, C. Barriers and Facilitators to Cervical Cancer Screening in High Incidence Populations: a synthesis of qualitative evidence. **Women Health,** v. 56, n. 4, p. 448-467, 2016.

DUNBERGER, G.; ALEVRONTA, E.; JOHANSSON, K.; OLSSON, C.; LIND, H.; WALDENSTRO, A.; STEINECK, G. Late symptoms in long-term gynaecological cancer survivors after radiation therapy : a population-based cohort study. **British Journal of Cancer,** v. 105, p. 737–745, set 2011.

FAUBION, S. S.; MACLAUGHLIN, K. L.; LONG, M. E.; PRUTHI, S.; CASEY, P. M. Surveillance and Care of the Gynecologic Cancer Survivor. **Journal of Women's Health**, v. 24, n. 11, p. 899–906, 2015a.

FAUBION, S. S.; MACLAUGHLIN, K. L.; LONG, M. E.; PRUTHI, S.; CASEY, P. M. Surveillance and Care of the Gynecologic Cancer Survivor. **Journal of Women's Health**, 2015b.

FERLAY, I. *et al.* Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. **International Journal of Cancer,** v. 5, n. 136, p. 359-386, mar 2015.

FLAY, L. D.; MATTHEWS, J. H. L. The effects of radiotherapy and surgery on the sexual function of women treated for cervical cancer. **International Radiation Oncology, Biology, Physics**, v. 31, n. 2, p. 399–404, 1995.

FRIGATO, S. HOGA, L. A. K. Assistência à mulher com câncer de colo uterino: o papel da enfermagem. **Revista Brasileira de Cancerologia**, v. 49, n. 4, p. 209–214, 2003.

HATA, M.; KOIKE, I.; MIYAGI, E.; NUMAZAKI, R.; ASAI-SATO, M.; KASUYA, T.; KAIZU, H.; MATSUI, T.; HIRAHARA, F.; INOUE, T. Radiation therapy for pelvic lymph node metastasis from uterine cervical cancer. **Gynecologic Oncology**, v. 131, n. 1, p. 99–102, 2013.

HENTSCHELL, H. *et al.* Validação do Female Sexual Function Index (FSFI) para uso em língua portuguesa. **Revista HCPA**, v. 1, n. 27, p. 10-14, 2007.

HOFSJÖ, A.; BOHM-STARKE, N.; BLOMGREN, B.; JAHREN, H.; BERGMARK, K.; HOFSJÖ, A.; BOHM-STARKE, N.; BLOMGREN, B.; JAHREN, H.; BERGMARK, K. Radiotherapy-induced vaginal fibrosis in cervical cancer survivors. **Acta Oncologica**, v. 0, n. 0, p. 000, 2017.

HUANG, Z.; ZHENG, Y.; WEN, W.; WU, C.; BAO, P.; WANG, C.; ZHONG, W.; GAO, Y. T.; JIN, F.; XIANG, Y. B.; SHU, X. O.; BEEGHLY-FADIEL, A. Incidence and mortality of gynaecological cancers: Secular trends in urban Shanghai, China over 40 years. **European Journal of Cancer**, v. 63, p. 1–10, 2016.

INSTITUTO NACIONAL DE CâNCER JOSÉ ALENCAR GOMES DA. **Estimativa 2018-incidência de câncer no brasil**. [s.l: s.n.]

INSTITUTO NACIONAL DE CâNCER JOSÉ ALENCAR GOMES DA SILVA. **DIRETRIZES brasileiras para o rastreamento do câncer do colo do útero**. [s.l: s.n.]

INSTITUTO NACIONAL DO CÂNCER. Neoplasia Intra Epitelial Cervical**. CIN**. **Revista**, v. 46, n. 4, p. 355–357, 2000.

JOO, E.; LIM, J.; WOO, U.; BEOM, Y. Gynecologic Oncology Effect of a pelvic fl oor muscle training program on gynecologic cancer survivors with pelvic fl oor dysfunction : A randomized controlled trial. **Gynecologic Oncology**, v. 125, n. 3, p. 705–711, 2012.

KIRCHHEINER, K.; NOUT, R. A.; LINDEGAARD, J. C.; HAIE-MEDER, C.; MAHANTSHETTY, U.; SEGEDIN, B.; JÜRGENLIEMK-SCHULZ, I. M.; HOSKIN, P. J.; RAI, B.; DÖRR, W.; KIRISITS, C.; BENTZEN, S. M.; PÖTTER, R.; TANDERUP, K. Dose-effect relationship and risk factors for vaginal stenosis after definitive radio(chemo)therapy with image-guided brachytherapy for locally advanced cervical cancer in the EMBRACE study. **Radiotherapy and Oncology**, v. 118, n. 1, p. 160–166, 2016.

LANCASTER, L. Preventing vaginal stenosis after brachytherapy for gynaecological cancer: An overview of Australian practices. **European Journal of Oncology Nursing**, v. 8, n. 1, p. 30–39, 2004.

LIND, H. *et al.* Late symptoms in long-term gynaecological cancer survivors after radiation therapy: a population-based cohort study. **British Journal of Cancer,** n. 105, p.737 – 745, 2011.

MAHMUD, A.; BRYDON, B.; TONITA, J.; HANNA, T. P.; SCHMIDT, M.; TAI, P. A population-based study of cervix cancer: Incidence, management and outcome in the canadian province of saskatchewan. **Clinical Oncology**, v. 23, n. 10, p. 691–695, 2011.

MARTIN, M.; LEFAIX, J.-L.; DELANIAN, S. TGF- □ 1 AND RADIATION FIBROSIS : A MASTER SWITCH AND A SPECIFIC THERAPEUTIC TARGET ? **International Journal of Radiation Oncology Biology Physics**, v. 47, n. 2, p. 277–290, 2000.

MILES, T.; JOHNSON, N. Europe PMC Funders Group Vaginal dilator therapy for women receiving pelvic radiotherapy. **The Cochrane Database of Systematic Reviews**, n. July 2010, 2014.

MINISTÉRIO DA SAÚDE. **Diretrizes brasileiras para o rastreamento do câncer do colo do útero**. [s.l: s.n.]

MOHAMED, S.; LINDEGAARD, J. C.; DE LEEUW, A. A. C.; JÜRGENLIEMK-SCHULZ, I.; KIRCHHEINER, K.; KIRISITS, C.; PÖTTER, R.; TANDERUP, K. Vaginal dose de-escalation in image guided adaptive brachytherapy for locally advanced cervical cancer. **Radiotherapy and Oncology**, v. 120, n. 3, p. 480–485, 2016.

MOHANTY, G. Risk factors for cancer of cervix, status of screening and methods for its detection. **Archives of Gynecology and Obstetrics,** v. 291, n. 2, p. 247-249, 2015.

MORRIS, L. *et al.* Radiation-induced vaginal stenosis: current perspectives. **International Journal of Women's Health,** v. 9, p. 273–279, 2017.

NATIONAL INSTITUTE OF CANCER. Common Terminology Criteria for Adverse Events ( CTCAE ). **NIH Publication**, v. 2009, p. 0–71, 2010.

OLIVEIRA, A.; SILVA, D. A.; POR, S.; CARLO, M. Comparação da dose absorvida no tratamento do cancer ginecologico por. 2010.

OLSON, B.; GRIBBLE, B.; DIAS, J.; CURRYER, C.; VO, K.; KOWAL, P.; BYLES, J. Cervical cancer screening programs and guidelines in low- and middle-income countries. **International Journal of Gynecology and Obstetrics**, v. 134, n. 3, p. 239–246, 2016.

PARK, H. S.; RATNER, E. S.; LUCARELLI, L.; POLIZZI, S.; HIGGINS, S. A.; DAMAST, S. Predictors of vaginal stenosis after intravaginal high-dose-rate brachytherapy for endometrial carcinoma. **Brachytherapy**, v. 14, n. 4, p. 464–470, 2015.

PETRY, K. U. HPV and cervical cancer. **Scandinavian Journal of Clinical and Laboratory Investigation**. v. 5513, 2014.

PHILLIPS, K.; HERSCH, J.; TURNER, R.; JANSEN, J.; MCCAFFERY, K. The influence of the 'cancer effect' on young women's responses to overdiagnosis in cervical screening. **Patient Education and Counseling**, v. 99, n. 10, p. 1568–1575, 2016.

POLAT, M.; KAHRAMANOGLU, I.; SENOL, T.; SENTURK, B.; OZKAYA, E.; KARATEKE, A. Hysterectomy on Lower Urinary Tract Function. **Journal Of**

**Laparoendoscopic & Advanced Surgical Techniques**, v. 26, n. 2, p. 116–121, 2016.

RAKHRA, S. S.; WEAVER, C.; DONNELLY, E. D.; HELENOWSKI, I.; PRESCOTT, A. E.; STRAUSS, J. B. The effect of pelvic radiotherapy on vaginal brachytherapy cylinder diameter: Implications for optimal treatment order. **Brachytherapy**, v. 15, n. 5, p. 549–553, 2016.

RAMASESHAN, A. *et al.* Pelvic floor disorders in women with gynecologic malignancies: a systematic review. **International Urogynecologycal Journal,** v. 29, n. 4, p. 459-476, 2018.

RAM ABHINAV, K.; JANAKI, M. G.; ARUL PONNI, T. R.; KIRTHI KOUSHIK, A. S.; MOHAN KUMAR, S.; RAM CHARITH, A.; RITIKA, H.; ARVIND, S. Analysis of Late Radiation Proctitis Among Patients Treated for Cervical Cancer: A Comparative Study Between Linear Accelerator and Cobalt Teletherapy. **Clinical Ovarian and Other Gynecologic Cancer**, v. 6, n. 1–2, p. 46–49, 2013.

RODEMANN, H. P.; BAMBERG, M. Cellular basis of radiation-induced fibrosis. Radiother Oncol. V. 35, n. 2, p. 83-90, 1995.

ROSA, L. M. da; HAMMERSCHMIDT, K. S. de A.; RADÜNZ, V.; ILHA, P.; TOMASI, A. V. R.; VALCARENGHI, R. V.; ROSA, L. M. da; HAMMERSCHMIDT, K. S. de A.; RADÜNZ, V.; ILHA, P.; TOMASI, A. V. R.; VALCARENGHI, R. V. Evaluation and Classification of Vaginal Stenosis After Brachytherapy. **Texto & Contexto - Enfermagem**, v. 25, n. 2, p. 1–8, 2016.

RUTLEDGE, T. L.; HECKMAN, S. R.; QUALLS, C.; MULLER, C. Y.; ROGERS, R. G. Pelvic floor disorders and sexual function in gynecologic cancer survivors : a cohort study. **YMOB**, v. 203, n. 5, p. 514.e1-514.e7, 2010.

SIEGEL, R. L.; MILLER, K. D.; JEMAL, A. Cancer Statistics, 2018. **CA Cancer Journal Clinical**, v. 68, n. 1, p. 7-30, 2018.

SILVA, M. P. P. e; GANNUNY, C. S.; AIELLO, N. A.; HIGINO, M. A. R.; FERREIRA, N. D. O.; OLIVEIRA, M. M. F. de. Métodos Avaliativos para Estenose Vaginal Pós-Radioterapia Assessment Methods for Post Radiotherapy Vaginal Stenosis. **Revista Brasileira de Cancerologia**, v. 56, n. 1, p. 65–70, 2010.

SIMÕES, R. B. **Evolução pós-conização por lesão intraepitelial de alto**. 2012.

SOARES, E. M.; SILVA, S. R. da. Perfil de pacientes com câncer ginecológico em tratamento quimioterápico. **Rev Bras Enferm**, v. 63, n. 4, p. 517–522, 2010.

STEWART, B. W.; WILD, C. P. World cancer report 2014. **World Health Organization**, p. 1–2, 2014.

SUH, D. H. *et al.* Major clinical research advances in gynecologic cancer in 2017. **Journal of Ginecologic Oncology,** v. 29, n. 2, 2018.

TAVARES, C. M. A.; PRADO, M. L. Do. Pesquisando a prevenção do câncer ginecológico em Santa Catarina. **Texto & Contexto - Enfermagem**, v. 15, n. 4, p. 578–586, 2006.

TORRE, L. A. *et al.* GLOBAL Cancer Statistics, 2012. **CA Cancer Journal Clinica**l, v. 65, n. 1, p. 87-108, 2015.

THOMAS, G.; DEMBO, A.; ACKERMAN, I.; FRANSSEN, E.; BALOGH, J.; FYLES, A.; LEVIN, W. A randomized trial of standard versus partially hyperfractionated radiation with or without concurrent 5-fluorouracil in locally advanced cervical cancer. **Gynecologic Oncology**, v. 69, n. 2, p. 137–145, 1998.

VISWANATHAN, A.N.; THOMADSEN, B. American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: General principles. **Brachytherapy,** v.11, p. 33-46, 2012

National Cancer Control Programmes: policies and manageriel guidelines. Geneva, WHO, 2002.

WOLF, J. K. Radiation Therapy. **October**, n. October, p. 665–671, 2006.

WHO. WORLD CANCER REPORT 2014. Lyon, 2014.

YANG, E. J. *et al.* Effect of a pelvic floor muscle training program on gynecologic cancer survivors with pelvic floor dysfunction: A randomized controlled trial. **Gynecologic Oncology,** v. 125, p. 705-711, 2012.

YOSHIDA, K. *et al.* Role of vaginal pallor reaction in predicting late vaginal stenosis after high-dose-rate brachytherapy in treatment-naive patients with cervical cancer. **Journal of Gynecologic Oncology**, v. 26, n. 3, p. 179-184, 2015.

ZOMKOWSKI, K.; TORYI, A. M.; SACOMORI, C.; DIAS, M.; SPERANDIO, F. F. Sexual function and quality of life in gynecological cancer pre- and post-short-term brachytherapy: a prospective study. **Archives of Gynecology and Obstetrics**, v. 294, n. 4, p. 833–840, 2016.

# 4 ARTICLE

**TO BE SUBMITTED TO THE ARCHIVES OF GYNECOLOGY AND OBSTETRICS JOURNAL**

Impact factor: 2.090 / Qualis: B1 (area 21)

## EFFECT OF THE VAGINAL DILATATOR ON THE VAGINAL DIMENSIONS AFTER GYNECOLOGICAL BRACHYTHERAPY- RANDOMIZED CLINICAL TRIAL

Taís Marques Cerentini[1,6], Júlia Schlöttgen[2,6,] Patrícia Viana da Rosa[3,6], Salvatore Giovanni Vitale[4,7], Fabrício Edler Macagnan[5,6]

[6] Federal University of Health Sciences of Porto Alegre(UFCSPA);

[7]University of Messina, University of Catania

[1]ORCID: 0000-0002-7300-4032; E-mail:taismcerentini@gmail.com;

[2]ORCID: 0000-0002-4981-5329E-mail:juliaschlottgen@gmail.com;

[3]ORCID: 0000-0001-9067-0718; E-mail:patriciarosa@ufcspa.edu.br;

[4]ORCID: 0000-0001-6871-6097; E-mail: salvatoregiovanni.vitale@unime.it

[5]ORCID: 0000-0002-8209-0251; E-mail: fmacagnan@gmail.com

Corresponding author: Taís Marques Cerentini

phone: +55 51 98108.2948

Email: taismcerentini@gmail.com

**Abstract**

*Objective*: To evaluate the dimensions of the vaginal canal in patients undergoing gynecological brachytherapy and the effect of the use of vaginal dilators (VD) used in the follow-up of pelvic physiotherapy. *Methods:* This is a randomized clinical trial in which 88 patients were allocated randomly in the control (CG: n = 32) and intervention (IG: n = 56) groups. Three evaluations were performed: pre-brachytherapy, post-brachytherapy and follow-up of 3 months. The CG received standard guidance from the health team while IG was instructed to use VD for three months. The dimensions of the vaginal canal (main outcome) were defined by the length of the vagina (cm), width (number of full clockwise turns of the opening thread in the gynecological speculum) and area (defined by the size of the VD). Quality of life (QOL) and pelvic floor (PF) functionality were also evaluated. *Results:* There was no effect of the VD on vaginal length ($p = 0.111$), width ($p = 0.490$) and area ($p = 0.743$). In the analysis stratified by adhesion, the CG had a significant decrease in the vaginal area ($p = 0.046$). PF was predominantly hypoactive (CG: 59.4%, IG: 69.9%) throughout the follow-up. QoL improved in both groups, but the reduction of constipation, vaginal dryness, and stress urinary incontinence manifested only in IG. *Conclusion:* The use of VD did not alter the dimensions of the vaginal canal within the first three months after the end of RT treatment for cervical cancer. However, there was a large sample loss during follow-up and therefore, studies with a larger sample number and longer follow-up time need to be conducted to evaluate the benefit of VD on vaginal dimensions, PF functionality and clinical evolution.

*Keywords:* Radiotherapy; Vaginal Dilators; Cervical Cancer; Pelvic Physiotherapy; Brachytherapy

## Introduction

Cervical cancer is the seventh most common cancer in the world, especially in regions with a low Human Development Index (HDI) where it is associated with 7.5% of cancer deaths [1]. In spite of this, incidence and mortality rates declined over the years due to screening programs, early detection and new approaches to treatment [2,3], resulting in a 5-year survival increase [4]. The treatment of advanced tumor varies according to the degree of the disease staging, and consists of the application of external irradiation to the pelvis and /or intracavitary and neoadjuvant chemotherapy [5]. Radiotherapy associates two techniques of application and has been considered fundamental for the increase in rates of recurrence-free survival [6-8]. Its external form should be applied within 8 weeks from IIB2> 4 cm staging or IIA with total dose intensities from 45 Gy to 50 Gy fractionally applied at 1.8 Gy or 2 Gy, usually by administering the concomitant cisplatin chemotherapy . In contrast, brachytherapy is performed intracavitary, accessing the uterus and offering lower irradiation rates for neighboring organs with 7 Gy planning once a week for up to 4 weeks [9]. However, the use of ionizing radiation induces difficult-to-resolve adverse effects that may adversely interfere with treatment [10].

The adverse effects of the radiotherapy treatment can start early in the first applications and extend for years, due to the genetic alterations that the ionization usually promotes. Acute effects are all clinical manifestations that occur within the first three months after treatment [11,12], where the most frequent are gastrointestinal and genitourinary [12]. In addition, the radiation causes damage to the vaginal epithelium, which may reduce tissue vascularization leading to pallor of the vaginal mucosa, loss of lubrication and inflammation [7,13-15]. This inflammatory process is associated with posterior fibrosis of muscle fibers and mucosal atrophy [7], which may result in narrowing of the vaginal canal [16-18]. These effects are intensified with the use of brachytherapy where larger doses are locally applied [19]. Often, in these clinical situations, there are narrowing of the vaginal canal that prevents the continuation of treatment by brachytherapy, gynecological exams and maintenance of sexual activity [19].

The variation in the dimensions of the vaginal canal leads to different degrees of vaginal stenosis [5]. Aiming to minimize the effects that the radiotherapy treatment promotes on the vaginal dimensions, the use of dilators [20-23] have been widely used [5,22]. However, use is limited by psychological barriers [15] and there is still a lack of evidence demonstrating the benefits of using this technique on vaginal dimensions, pelvic floor functionality, clinical signs and symptoms, and quality of life [15,24]. Therefore, the objective of this study is to evaluate the effect of the use of vaginal dilators (VD) on the vaginal canal dimensions of patients undergoing gynecological brachytherapy. As secondary endpoints, the effect of VD on pelvic floor functionality, clinical signs and symptoms and quality of life was evaluated.

## Methods

In this randomized clinical trial, 88 women with cervical cancer were assigned to radiotherapy. The study was approved by the research ethics committee (CAAE: 63083516.4.0000.5335) and duly registered

with ClinicalTrials (NCT: 03090217). All the volunteers received and signed the given consent form (TCLE) in accordance with the regulations in force in the national legislation and in line with the Helsinki declaration. All patients were invited to participate in the study, who at the end of radiotherapy treatment by teletherapy were referred to the intracavitary irradiation sessions of gynecological brachytherapy. To participate in the study, the dimensions of the vaginal canal at the initial pre-brachytherapy evaluation should be considered normal.

**Fig 1** 1 Diagram according to the guideline established by CONSORT (Consolidated Standards of ReportingTrials)

*Assessments*

A trained physiotherapist evaluated the volunteers at three times: 1) before the first brachytherapy session, 2) at the last brachytherapy session, and 3) three months after the end of treatment (figure 2). Clinical and sociodemographic evaluation was initially performed, followed by determination of vaginal canal dimensions, pelvic floor examination and quality of life. The determination of vaginal canal size included evaluation of length, width and area. The vaginal length (cm) was determined using a hysterometer, using the posterior fornix of the vagina as the starting point, and the hymenal ring as the end point. The width of the vagina was measured using vaginal dilators (DV). Different graduations of VD of the brand 'A Sós □' were used. For this, different VDs were inserted, in ascending order of size. The size setting should result from the largest VD capable of being inserted and maintained without pain, tightening or bleeding for at least 3 minutes. The measurements of the height and width of the VD, according to the values indicated by the manufacturer of the device, were used to calculate the area of the vagina (cm2). Measurement of the width of the vagina was determined through the opening of the vaginal speculum. To do this, in the horizontal position, a number one acrylic speculum was introduced into the vagina. During the opening of the speculum, each clockwise half-turn given on the thread was registered. The total number of half-rounds was used as the width measurement parameter. The opening of the speculum was limited by mechanical restriction or by the manifestation of pain. The kinesiological-functional diagnosis of the pelvic floor (KFD-PF) was performed through bidigital palpation. A endurance and power of this musculature was determined as proposed by Bernards et al. [25]. The classification of the activity of this musculature followed the recommendations proposed by Masselink et al. [26] and were stratified into: 1) hypoactive (PF muscle inability to contract voluntarily and involuntarily when necessary) 2) normal (ability of PF muscles of normal or strong voluntary contraction and complete voluntary relaxation, in addition to pre-contraction present) and 3) hyperactive (the pelvic floor muscles do not relax, or may even contract when relaxation is functionally needed); The quality of life was assessed by the Quality of Life Assessment questionnaire of the general neoplasia patient proposed by the EuropeanOrganization for Research and Treatment - Cancer - EORTC QLQ-C30 [27].

**Fig 2** Study timeline

*Allocation and masking*

The volunteers eligible to participate in the study were randomly assigned to the control group (CG) or intervention (IG). In the CG, the volunteers received only the usual orientations of the nursing team and participated in all the evaluations foreseen in the study. In the IG, the volunteers received the VD and all necessary guidelines of use. The VD size was defined at the initial evaluation and each volunteer received the device with the size compatible with the individual anatomical conditions. The early initiation of the use of VD, that is, concomitantly with brachytherapy, was evaluated in a subgroup of volunteers. However, the statistical analysis showed that the early use of these VDs did not promote any difference in the vaginal dimensions and therefore, the IG was composed of volunteers who used the VD at the beginning of the brachytherapy (n = 23) and volunteers who only started after the end of the brachytherapy (n = 34). Thus the allocation ratio resulted in 1 volunteer in CG for 02 in IG.

*Treatment*

Radiotherapy treatment was determined by the care routine that takes into account the patient's clinical peculiarities and the degree of tumor staging. The minimum radiation dose used was 45 Gy and the maximum dose was 50.4 Gy, divided from 25 to 28 fractions (sessions) of 1.8 Gy. The sessions were conducted daily by teletherapy. At the end of the teletherapy, the volunteers were referred to the intracavitary irradiation sessions by gynecological brachytherapy, performed according to the protocol of the radiotherapy service (from a Center of High Complexity of the South of Brazil - CACON) using GammaMedplus ™ iX HDR / PDR Brachytherapy Afterloader with iridium 192, guided by X-ray image. The dose used was 7 Gy divided into 4 fractions applied once a week, applied through rings and /or cylinders. It was recommended to abstain from sexual activities after the beginning of brachytherapy until the fourth week of the end of the intracavitary irradiation. he use of VDs was individual and the patients were oriented to use the device for three months, four times a week and for 10 to 15 minutes each time. The VDs were given to the patients following the stipulation of vaginal size on the first evaluation.

*Statistical methods*

The qualitative data were presented in frequency and percentage, while the quantitative data by mean, median, standard deviation, standard error and interquartile range, according to the normal distribution of the values. Normality was assessed by the Shapiro-Wilk test. Comparisons between groups were performed using Student's t-test or the Wilcoxon-Mann-Whitney test. Associations were found by the chi-square test or Fisher's exact test, while correlations were identified by Spearman's correlation test. Comparisons between moments and between groups were evaluated using generalized estimation equations (GEE) models with Bonferroni post-hoc tests according to the intention-to-treat (ITT) method. The statistical significance in use was 5% ($p < 0.05$) and the analyzes were done in SPSS software version 23.

**Results**

One hundred and one patients were evaluated for eligibility. Of these, 12 were excluded because they did not meet the inclusion criteria or because they did not agree to participate in the study. The sample consisted of 88 women (43.7 ± 11.9 years) randomized to CG (n = 32) and IG (n = 56). During the follow-up, there was loss due to death, withdrawal and need for hospitalization (figure 1). Of the total sample, 33% (n = 29) of the volunteers were postmenopausal, 66% (n = 58) were sexually active, of which 66% (n = 38) used some contraceptive method. Predominantly, the degree of involvement of the sample was diagnosed with staging IIB (45.5%) and squamous cell carcinoma (89.8%). There was little exposure to tobacco (10%) and alcohol (1%). Clinical variables were symmetrically distributed between groups except for the therapeutic regimen used in the pre-brachytherapy period. As described in table 1, in the CG there was a higher number of conization when compared to the IG.

**Table 1** Characterization of the sample

Adherence to the protocol declined with follow-up and there was a high rate of loss throughout the study (post-brachytherapy loss / CG: n = 10, IG: n = 14; loss at 3-month follow-up CG: n = 13, IG : n = 25), but this behavior was similar between the groups (x2 = 0.146, p = 0.702). The results of multivariate analyzes showed that adherence was not significantly influenced by age (p = 0.461), origin (p = 0.295), marital status (p = 0.243), schooling (p = 0.619), number of pregnancies ), clinical diagnosis (p = 0.726), disease staging (p = 0.373), pre-brachytherapy regimen (p = 0.353) and sexual behavior (p = 0.815). However, in women with hypoactive pelvic floor there was a tendency of less adherence to follow-up (p = 0.070).

The dimensions of the vaginal canal were measured by three different measures: length (in centimeters), width (number of turns in the gynecological speculum) and area (in $cm^2$). In the multivariate analysis no intervention effect was observed for any of the vaginal canal size variables (length: F = 2,545, p = 0,111, width: F = 0,490, p = 0,484, area: F = 0,107, p = 0,743). There was also no interaction between intervention and time for the variables width and area (width: F = 1,135, p = 0,567 and area: F = 3,228, p = 0,199). However, there was interaction between intervention and time in the variable length (F = 6.286, p = 0.043), in which the basal vaginal length values were lower in the CG (6.6 ± 0.19 cm vs 7.3 ± 0.16 cm, p = 0.011). This difference remains in the post-brachytherapy evaluation (CG: 6.6 ± 0.22 cm; IG: 7.3 ± 0.17 cm; p = 0.003), but it reduces at the end of follow-up (CG: 7 , 2 ± 0.29 cm, IG: 6.9 ± 0.26 cm, p = 0.377) as shown in figure 3. In the analyzes where conization was treated as covariate, the results were maintained, demonstrating that, independently of clinical conditions, the treatment did not significantly alter vaginal dimensions. The same was observed when we tested the influence of signs and symptoms related to the treatment of gynecological cancer. When stratifying the results of the volunteers who participated in all the proposed evaluations (CG: n = 9 and IG: n = 17), we did not find effect of the use of dilators on vaginal

length and width (F = 0.206; p = 0.614; F = 0.917, p = 0.348). However, in the CG there was a significant reduction in the vaginal area at the end of the segment (p = 0.046).

**Fig 3** A follow-up of vaginal canal measurements in the groups throughout the protocol (a - vaginal length with follow-up; b-vaginal width with follow-up; c-vaginal area with follow-up)

The KFD-PF result was similar between the groups at baseline assessment (baseline CG: 59.4% hypoactive, 12.5% hyperactive, 28.1% normal, IG: 69.6% hypoactive, 14.3% hyperactive, 16.1% normal) and there was no significant alteration of the diagnoses during follow-up (X2 = 3.119, p = 0.210). Similar behavior was observed in the clinical signs and symptoms commonly manifested in patients undergoing gynecological cancer treatment. Both prevalence and incidence were similar between groups for most of the clinical findings, and there were no treatment effects (X2 = 1.909, p = 0.167) and time (X2 = 0.548, p = 0.760) on the number however, when we analyzed the clinical occurrences only in the women who completely completed the evaluations foreseen in the protocol, we identified that in IG there was a significant reduction in constipation and vaginal dryness at the end of follow-up A relevant fact is that in the stratified analyzes, SUI remained lower in the IG as described in table 2.

**Table 2** Control of occurrence of clinical signs and symptoms in analysis stratified by adherence

The overall quality of life assessment score was similar between the groups throughout the follow-up (X2 = 0.007, p = 0.936). Likewise, domains that evaluated aspects related to functional quality and clinical symptoms were similar between groups (X2 = 0.001, p = 0.973, X2 = 0.152, p = 0.666, respectively), all domains improved at the end of (domain global: X2 = 5.995, p = 0.05, functional domain: X2 = 24,767, p = 0.001, domain symptoms: X2 = 17,077, p = 0.001), as described in table 3. Only in the functional domain, the effect of time was significant in isolated intragroup analyzes.

**Table 3** Quality of life

The results demonstrated that there were no associations between the KFD-PF and the length and area of the vaginal canal. On the other hand, women with hypoactive PF had a significant decrease in vaginal width (p = 0.042). Regarding quality of life (QLQ-C30), significant improvement in the overall health domain was observed throughout the follow-up and occurred independently of the KFD-PF. However, women with hyperactive pelvic floor presented significant improvement in quality of life (p = 0.006), whereas in the symptom domain, there was a significant worsening in the cases of PF hypoactivity (p = 0.006). In the analysis stratified by adherence, the association between KFD-PF and the QLQ-C30 domains was also similar to those observed in the statistical treatment of intention to treat. The total number of occurrences of clinical signs and symptoms did not influence the quality of life. However, in the isolated or combined

presence of vaginal discharge, urinary retention, diarrhea and edema, there was a lower score in the functional domain ($x^2$: 3.842; p = 0.050; $x^2$: 7.839; p = 0.005; $x^2$: 3.766; p = 0.05; 4,731, p = 0.30, respectively). Vaginal dryness and constipation negatively influenced the symptoms domain ($x^2$: 5.597; p <0.18; $x^2$: 8.032; p = 0.005, respectively). There was also a negative association between constipation and overall quality of life ($x^2$: 6.027; p = 0.049).

**Discussion**

The objective of this study was to evaluate the behavior of the vaginal canal dimensions during the first three months of the end of the RT followed by gynecological brachytherapy to determine the possible benefits of the use of vaginal dilators that have been used in the monitoring of pelvic physiotherapy. At the end of the follow-up, we observed that there was no difference between the intervention and control groups in relation to the variables used in the determination of vaginal dimensions, as well as no effect of the intervention on quality of life, signs and symptoms, and KFD-PF.

The random formation of the groups guaranteed similarity in the clinical conditions between the groups, but there was a significant difference in relation to the therapeutic scheme used in cancer treatment. The prevalence of conization was higher in the control group, but in the stratified analysis this condition did not significantly interfere with the dimensions of the vaginal canal. Adherence to the protocol was considerably low and declined with follow-up in both groups. Only 28% of the women performed the final evaluations in the CG and 30% in the IG. This difficulty of adherence is reported by different health professionals who handle women with cervical cancer [28,29]. We did not identify any predictive factors for these losses, but women with pelvic floor hypoactivity, tendentiously was lower, corroborating with the findings of Rutledge [30] that obtained greater agreement to the protocols proposed in volunteers with better PF muscle activity. However, even if our data are not sufficiently conclusive, it is presumed that the preservation of PF muscle activity influenced the adherence, since in the domain of symptoms and functional quality of the quality of life questionnaire, the results were less favorable in women with a diagnosis of hypoactivity of this musculature. In addition, the number of occurrence of signs and symptoms was higher in these women. It is possible that the strength of the PF is a reflection of the degree of body consciousness. Self-knowledge and self-care may, as proposed by Carter et al. [31], directly influence adherence to prevention programs and gynecological treatments and thus justify, at least in part, the results of our study.

The disorders resulting from brachytherapy treatment affect 30% of uterine cancer survivors [32], and impairments to quality of life tend to begin to improve 3 to 6 months after the end of RT [33]. This pattern of clinical response was evidenced in our findings, since quality of life improved significantly at the end of the follow up. Leeuwn et al. [34] followed the evolution of QoL in pelvic cancer survivors and found that the domains of functional quality and severity of symptoms improved significantly one year after the end of treatment. However, improvement in QOL was not influenced by treatment (use of dilators) and the effect of time was significant only when the data were grouped into a single group. This implies that it is

enough to terminate the treatment for gynecological cancer so that the QoL improves, so much that in the intragroup analysis, the CG had significant improvement in the functional quality.

Even with important deleterious effects, RT increases survival rates [35]. These effects arise from the involvement of healthy cells that are located around the irradiated region and the degree of reaction is directly dependent on the tissue sensitivity and dose used in the treatment [36]. The proportion of clinical signs and symptoms observed in volunteers in both groups was similar to the findings previously described by Ramaseshan et al. [35], where the acute effects that appear more frequently in the treatment of gynecological cancer involve from genitourinary, gastrointestinal and alterations of the vaginal mucosa including the presence of dryness, edema and the presence of scars. However, at the end of the follow up, there was a lower incidence of constipation, dryness and SUI in the treated group. Carter et al. [31] sought to evaluate the benefits of vaginal and sexual health treatment strategies and found that the resources used to improve hydration and flexibility of the vaginal mucosa and the use of VD as a means of developing awareness and proprioception of the pelvic floor were associated with the reduction of the symptoms resulting from treatment with gynecological RT.

However, our findings demonstrate that the use of VD did not modify vaginal canal size three months after RT, and these results suggesting that early use of dilators for the prevention of vaginal narrowing does not induce short-term benefits. On the other hand, there are indications that the use of VD can prevent vaginal narrowing as previously described [37-40]. In the observational and uncontrolled study by Velaskar et al. [37], vaginal canal length (average = 6 cm after 6-10 weeks of RT termination) was shown to increase with the use of VD (average = 9 cm after 4 months of vaginal dilation therapy). In this study, 89 women with cervical cancer treated with RT applied in the mode of teletherapy were included. Miles et al. [41] measured vaginal length and elasticity and found that the use of VD did not significantly alter these measures. Bahng et al. [38] observed in patients submitted to brachytherapy the orientation of the daily use of VD (from 2 weeks after the end of RT),an increase in vaginal canal length (OR: 0.17). In relation to the vaginal area, the available information is scarce. Only a recent study [42] evaluated the vaginal diameter before and after the end of RT, and found a decrease of the area in only 11% of the evaluated sample. Similar results were observed in our study, where the vaginal area, evaluated through the size of the VD, remained practically constant throughout the follow up. However, in the stratified analysis by adherence, a reduction in the vaginal area of the women allocated to the CG was found at the end of the follow-up. The impact of RT on the vaginal area is poorly described in the literature. As far as we know, there is no randomized clinical trial testing the effect of VD use on the measure. In addition, the vaginal area measurement strategy we use is a method not mentioned in the literature. This limits the comparison with other studies.

Law et al. [39] evaluated vaginal size with a strategy similar to that proposed in this study. They studied the efficacy and adherence to the use of VD in patients oriented to use the dilators 3 times per week during 12 months, regardless of the number of sexual relations. At the initial assessment, vaginal canal size was determined from the largest dilator that could be inserted and maintained for 10 minutes without pain, tightness or bleeding. The efficacy of the treatment was defined when the dilator size was equal to the initial

evaluation. The authors observed that VD size was lower in 49% of the volunteers in the first month after the end of RT. However, during the study, 52% of the reductions were reversed in 6 months of treatment. Our follow up was only 3 months after the radiotherapy treatment and we had a high sample loss. Adherence to VD was not monitored as was sexual activity, which was released from the fourth week of brachytherapy completion. Therefore, this is a limitation found and the evidence raised in our study may be questionable and possibly different results than ours can be observed in situations with better adherence, since in the stratified analysis, we detected indications that the use of VD can help in the maintenance of the vaginal area, since in the CG there was a significant reduction of this measure.

Other limitations of our study that we can point out is the need to measure the dimensions of the vaginal canal before the start of teletherapy. However, most of the women referred to gynecological brachytherapy in this service begin treatment with RT in other oncological centers. This same factor may have affected adherence to the follow-up in virtue of the displacement. Another important issue was the difficulty in controlling adhesion to the use of the dilator, a problem that we face due to lack of feedback. In conclusion, the effect of VD use in the first three months after RT does not have an acute effect on the length, width and area of the vaginal canal of women with cervical cancer, but the low adhesion to the study makes it impossible to extrapolate our results to this population. However, there are indications that VD can contribute to the improvement of PF muscle function and benefit the clinical evolution of these women, but studies with greater sampling power and longer follow-up should be conducted to clarify the possible benefits of this technique of pelvic physiotherapy.

**Author contribution:** Cerentini TM: protocol/Project development, data collection and analysis, manuscript writing; Schlöttgen J:data collection; Vitale SG: manuscript editing; Rosa PV: protocol/Project development, manuscript editing; Macagnan FE: protocol/Project development, data analysis, manuscript writing and editing.

**Compliance with etical standards**

**Funding organization:** nothing to declare

**Conflict of interest** Taís Marques Cerentini, Julia Schlöttgen, Patrícia Viana da Rosa, Salvatore Giovanni Vitale and Fabrício Edler Macagnan declare that they have no conflict of interest.

**Ethical approval** This article does not feature any studies on animals performed by any of the authors. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and is later amendments or comparable ethical stardarts. Thys study is approved by the National Ethics Committee of the Irmandade Santa Casa de Misericórdia de Porto Alegre (ISCMPA) number 2.017.148.

**Informed consent** informed consent was obtained from all individual participants included in the study.

**References**


1. Stewart BW, Wild CP. (2014) World cancer report 2014. World Health Organization http://www.videnza.org/wp-content/uploads/World-Cancer-Report-2014.pdf. Acessed 14 June 2018
2. Smith RA, Andrews KS, Brooks D, et al. (2018) Cancer screening in the United States , 2018 : A Review of Current American Cancer Society Guidelines and current issues in cancer screening. CA Cancer J. Clin 00:1–20
3. American Cancer Society (2018) Cancer facts & figures 2018. Atlanta https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf. Acessed 14 June 2018
4. Ye S, Yang J, Cao D, Lang J, Shen K. (2014) A systematic review of quality of life and sexual function of patients with cervical cancer after treatment search strategy and inclusion criteria. Int J. Gynecol Cancer 24:1146–1157
5. Bakker RM, Mens JWM, Groot HE De (2017) A nurse-led sexual rehabilitation intervention after radiotherapy for gynecological cancer. Support. Care Cancer. http://dx.doi.org/10.1007/s00520-016-3453-2
6. Zomkowski K, Toryi AM, Sacomori C, Dias M, Sperandio FF (2016) Sexual function and quality of life in gynecological cancer pre- and post-short-term brachytherapy: a prospective study. Arch. Gynecol. Obstet. 294:833–840.
7. Kokka F, Bryant A, Brockbank E, Powell M, Oram D (2015) Hysterectomy with radiotherapy or chemotherapy or both for women with locally advanced cervical cancer Cochrane Database Syst Rev 4
8. ESMO Guidelines Committee (2018) Cervical cancer : Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. https://academic.oup.com/annonc/article-abstract/28/suppl_4/iv72/3958154. Acessed 14 June 2018
9. Miglierini P, Malhaire J, Goasduff G, Miranda O, Pradier O (2014) Cervix cancer brachytherapy : High dose rate. Cancer / Radiother. http://dx.doi.org/10.1016/j.canrad.2014.06.008
10. Mordhorst LB, Karlsson L, Ba ÞB, Sorbe B. (2014) Combined external and intracavitary irradiation in treatment of advanced cervical carcinomas predictive factors for treatment outcome and early and late radiation reactions. Int J. Gynecol Cancer 24:1268–1275
11. Wolf JK. (2006) Prevention and treatment of vaginal stenosis resulting from pelvic radiation therapy. Community oncol. J. 665–671.
12. Mouttet-audouard R, Lacornerie T, Tresch E, et al. (2015) What is the normal tissues morbidity following Helical Intensity Modulated Radiation Treatment for cervical cancer ? Radiother. Oncol. http://dx.doi.org/10.1016/j.radonc.2015.02.010
13. Delanian S, Lefaix J. The radiation-induced fibroatrophic process : therapeutic perspective via the antioxidant pathway. Semin Radiat Oncol 17: 99-107

14. Bruner DW, Nolte SA, Shahin MS, et al. (2006) Measurement of vaginal length: Reliability of the vaginal sound - A Gynecologic Oncology Group Study. Int. J. Gynecol. Cancer.16:1749–1755
15. Lee Y. (2018) Patients perception and adherence to vaginal dilator therapy: a systematic review and synthesis employing symbolic interactionism. Patient Preference and Adherence. 12: 551–560
16. Mohamed S, Lindegaard JC, de Leeuw AAC, et al. (2016) Vaginal dose de-escalation in image guided adaptive brachytherapy for locally advanced cervical cancer. Radiother. Oncol. http://dx.doi.org/10.1016/j.radonc.2016.05.020
17. Lancaster L. (2004) Preventing vaginal stenosis after brachytherapy for gynaecological cancer: An overview of Australian practices. Eur. J. Oncol. Nurs. 8:30–39
18. Park HS, Ratner ES, Lucarelli L, et al. (2015) Predictors of vaginal stenosis after intravaginal high-dose-rate brachytherapy for endometrial carcinoma. Brachytherapy 14: 464–470
19. Kirchheiner K, Nout RA, Lindegaard JC, et al. (2016) Dose-effect relationship and risk factors for vaginal stenosis after definitive radio(chemo)therapy with image-guided brachytherapy for locally advanced cervical cancer in the EMBRACE study. Radiother. Oncol. 116:160–166
20. Bakker RM, Vermeer WM, Creutzberg CL. (2015) Qualitative accounts of patients' determinants of vaginal dilator use after pelvic radiotherapy. J. Sex. Med. 12:764–773
21. Bergin R, Hocking A, Robinson T, et al. (2016) Continuing variation and barriers to nurse-led vaginal dilator education for women with gynaecological cancer receiving radiotherapy. Eur. J. Oncol. Nurs. 24:20–21.
22. Miles T, Johnson N (2010) Vaginal dilator therapy for women receiving pelvic radiotherapy: Types of outcome measures Primary outcomes. Cochrane Database Syst Rev 9:1–16
23. Cullen K, Fergus K, Dasgupta T, et al. (2013) Toward clinical care guidelines for supporting rehabilitative vaginal dilator use with women recovering from cervical cancer. Support. Care Cancer. 21:1911–1917
24. Morris L, Do V, Chard J, Brand AH (2017) Radiation-induced vaginal stenosis: Current perspectives. Int. J. Womens. Health. 9:273–279
25. Bernards ATM, Berghmans BCM. (2014) Dutch guidelines for physiotherapy in patients with stress urinary incontinence : an update. Int Urogynecol J. 25:171–179
26. Vartanian J, Carvalho A, Furia C. (2007) Questionários para a avaliação de qualidade de vida em pacientes com câncer de cabeça e pescoço validados no Brasil. Rev Bras Cir Cabeça e pescoço. 36:108–15
27. Messelink B, Benson T, Berghmans B, et al. (2005) Standardization of Terminology of Pelvic Floor Muscle Function and Dysfunction : Report From the Pelvic Floor Clinical Assessment Group of the International Continence Society. Neurourology and Urodynamics 24:374 - 380
28. Ely GE, White C, Jones K, et al (2014) Cervical Cancer Screening: Exploring Appalachian Patients' Barriers to Follow-Up Care. Soc Work Health Care 53: 83–95
29. Wordlaw-stinson L, Jones S, Little S, et al. (2014) Challenges and Recommendations to Recruiting Women Who Do Not Adhere to Follow-Up Gynecological Care. Open J Prev Med. 4: 123–128

30. Rutledge TL, Rogers R, Lee S, Muller CY. (2014) A pilot randomized control trial to evaluate pelvic floor muscle training for urinary incontinence among gynecologic cancer survivors. Gynecol Oncol. 132: 154–158
31. Carter J, Stabuke C, Seidel B, et al. (2017) Vaginal and Sexual Health Treatment Strategies within a Female Sexual Medicine Program for Cancer Patients and Survivors. J Cancer Surviv. 11: 274–283
32. Kirchheiner K, Czajka-pepl A, Ponocny-seliger E, et al. (2014) Posttraumatic stress disorder after high-dose-rate brachytherapy for cervical cancer with 2 fractions in 1 application under spinal / epidural anesthesia : incidence and risk factors. Int J Radiation Oncol Biol Phys. 89: 260-267
33. Pfaendler KS, Wenzel L, Mechanic MB, et al. (2015) Cervical cancer survivorship: Long-term quality of life and social support. Clin Ther. 37: 39–48.
34. Leeuwen M Van, Husson O, Alberti P, et al. (2018) Understanding the quality of life ( QOL ) issues in survivors of cancer : towards the development of an EORTC QOL cancer survivorship questionnaire. Health and Quality of Life Outcomes 16: 1–15
35. Ramaseshan AS, Felton J, Roque D, et al. (2017) Pelvic floor disorders in women with gynecologic malignancies : a systematic review. Int Urogynecol J.
36. Lind H, Waldenstro AC, Dunberger, et al (2011) Late symptoms in long-term gynaecological cancer survivors after radiation therapy : a population-based cohort study. British Journal of Cancer. 105: 737–745
37. Velaskar SM, Martha R, Mahantashetty U, Badakare JS, Shrivastava SK. (2007) Use of indigenous vaginal dilator in radiation induced vaginal stenosis. Indian J. of Occupational Therapy 34:3–6
38. Bahng AY, Dagan A, Bruner DW, Lin LL. (2012) Determination of prognostic factors for vaginal mucosal toxicity associated with intravaginal high-dose rate brachytherapy in patients with endometrial cancer. Int. J. Radiat. Oncol. Biol. Phys. 82:667–673
39. Law E, Kelvin JF, Thom B, et al. (2015) Prospective study of vaginal dilator use adherence and efficacy following radiotherapy. Radiother. Oncol. http://dx.doi.org/10.1016/j.radonc.2015.06.018
40. Ferlay J, Soerjomataram I I, Dikshit R, et al. (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. http://www.ncbi.nlm.nih.gov/pubmed/25220842 Acessed 14 June 2018
41. Miles T, Johnson N (2010) Vaginal dilator therapy for women receiving pelvic radiotherapy. Cochrane Database Syst Rev. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4171967/pdf/emss-57973.pdf Acessed 14 June 2018
42. Martins J, Francisca A, Regina V, et al. (2017) Factors associated with changes in vaginal length and diameter during pelvic radiotherapy for cervical cancer. Arch. Gynecol. Obstet. https://www.ncbi.nlm.nih.gov/pubmed/28975498. Acessed 14 June 2018

**Tables**

**Table 1** Characterization of the sample

| | GC (n=32) | GI (n= 56) | p-value |
|---|---|---|---|
| Age | 46,69 (14,06) | 42,03(10,24) | 0,078 |
| BMI | 26,39 (5,23) | 25,72 (6,18) | 0,603 |
| **Ethnicity** | | | >0,999* |
| Caucasian | 27 (84,4) | 48 (85,7) | |
| Afrodescendant | 5 (15,6) | 8 (14,3) | |
| **Marital status** | | | 0,326 |
| Married | 17 (53,1) | 27 (48,2) | |
| Divorced | 4 (12,5) | 8 (14,29) | |
| Single | 8 (25,0) | 20 (35,71) | |
| Widow | 3 (9,38) | 1 (1,79) | |
| **Schooling** | | | 0,799 |
| Elementary and middle school | 16 (50,0) | 24 (42,9) | |
| High School | 15 (46,9) | 29 (51,8) | |
| Higher Education | 1 (3,1) | 3 (5,4) | |
| **Clinical Diagnosis** | | | 0,333 |
| Adenocarcinoma of the uterine cervix | 1(3,1) | - | |
| Squamous cell carcinoma | 29 (90,6) | 50 (89,3) | |
| Granulocyte cell carcinoma | 2 (6,3) | 6 (10,7) | |
| **Staging** | | | 0,343 |
| IIA | 3 (9,4) | 2 (3,6) | |
| IVA | - | 1 (1,8) | |
| IB | 1 (3,1) | 5 (8,9) | |
| IIB | 12 (37,5) | 28 (50,0) | |
| IIIB | 16 (50,0) | 20 (35,7) | |
| **Pre-brachytherapy therapeutic scheme** | | | **<0,001** |
| Exclusive Teletherapy | 1 (3,1) | 2 (3,6) | |
| Teletherapy and conization | 4 (12,5) | 1 (1,8) + | |
| Teletherapy and chemotherapy | - | 21 (37,5) | |
| Teletherapy, conization and chemotherapy | 27 (84,4) | 32 (57,1) + | |
| **Treatment analysis** | | | **<0,001** |
| Chemotherapy | 27 (84,4) | 53 (94,6) | |
| Conization | 31 (96,9) | 33 (58,9) + | |
| **Received dose in teletherapy** | | | >0,999 |
| 45Gy | 11 (34,4) | 20 (57,7) | |
| 50,4Gy | 21 (65,6) | 36 (64,3) | |

Gy: intensity of radiation expressed in Grays; Data are expressed as average ± standard deviation of the average / absolute number of subjects and percentage number; * = Fischer exact test; + = Significant difference when compared to the control group.

**Tabela 2** Control of occurrence of signs and symptoms.

| | | **Basal** | **Post-Brachytherapy** | **3 months Follow-up** |
|---|---|---|---|---|
| **Urinary retention** | | | | |
| | CG | 5 (56) | 5 (56) | 4 (44) |
| | IG | 6 (35) | 6 (35) | 4 (23) |
| **Haematuria** | | | | |
| | CG | 0 | 0 | 0 |
| | IG | 0 | 1 (6) | 0 |
| **Emergency Urinary Incontinence** | | | | |
| | CG | 6 (67) | 4 (44) | 5 (55) |
| | IG | 7 (41) | 7(41) | 5 (29) |
| **Stress Urinary Incontinence** | | | | |
| | CG | 6 (67) | 4 (44) | 6 (67) |
| | IG | 5 (29) | 5 (29) | 2 (12) * |
| **Spontaneous bleeding** | | | | |
| | CG | 0 | 2 (22) | 2 (22) |
| | IG | 0 | 3 (18) | 1 (6) |
| **Vaginal discharge** | | | | |
| | CG | 3 (33) | 5 (56) | 6 (67) |
| | IG | 8 (47) | 7 (41) | 47 (43) |
| **Vaginal dryness** | | | | |
| | CG | 3 (33) | 1 (11) | 3 (33) |
| | IG | 6 (35) | 3 (18) | 9 (53) $^{+}$ |
| **Fetid odor** | | | | |
| | CG | 2 (22) | 2 (22) | 4 (44) |
| | IG | 4 (23) | 6 (35) | 6 (35) |
| **Constipation** | | | | |
| | CG | - | 2 (22) | 1 (11) |
| | IG | 4 (23) | 3 (18) | $0^{++}$ |

| | | | | |
|---|---|---|---|---|
| **Diarrhea** | | | | |
| | CG | 3 (33) | 4 (44) | 3 (33) |
| | IG | 5 (30) | 5 (30) | 2 (12) |
| **Scars** | | | | |
| | CG | 5 (36) | 4 (44) | 5 (56) |
| | IG | 4 (25) | 3 (18) | 6 (35) |
| **Edema** | | | | |
| | CG | 1 (11) | 1 (11) | 1 (11) |
| | IG | 2 (12) | 1 (6) | - |

The data are expressed in absolute number of occurrence of symptoms and in percentage number (%). Statistical analysis was performed according to the Chi-square procedures, stratified by adherence, where they were included only in the women who completed the follow-up (GC: n = 9; GI: n = 17). * = significant difference when compared to control. + = significant difference in relation to baseline assessment; ++ = significant difference in relation to post-brachytherapy evaluation.

**Tabela 3** : Quality of life

| **QLQC30** | | **Basal** | **Post-Brachytherapy** | **3 months Follow-up** |
|---|---|---|---|---|
| **Global** | | | | |
| | All | 73,9 ± 3,4 | 72 ± 3,7 | 78 ± 3,4+ |
| | CG | 74,5 ± 5,3 | 73 ± 5,6 | 79 ± 5,1 |
| | IG | 73,1 ± 3,1 | 74 ± 3,2 | 80 ± 4,1 |
| **Functional** | | | | |
| | All | 59 ± 3,7 | 65 ± 4,4* | 74 ± 4,3* |
| | CG | 58 ± 5,8 | 67 ± 7,2 | 74 ± 6,6+ |
| | IG | 60 ± 3,4 | 64 ± 3,5 | 74 ± 4,6* |
| **Symptoms** | | | | |
| | All | 38 ± 3,9 | 34 ± 3,9 | 24 ± 2,8* |
| | CG | 40 ± 6,2 | 36 ± 6,7 | 24 ± 4,5 |
| | IG | 37 ± 3,5 | 32 ± 3,0 | 24 ± 3,6 |

* = significant difference when compared to previous evaluations. + = significant difference when compared to baseline assessment. Data are expressed as mean ± standard deviation of the mean.

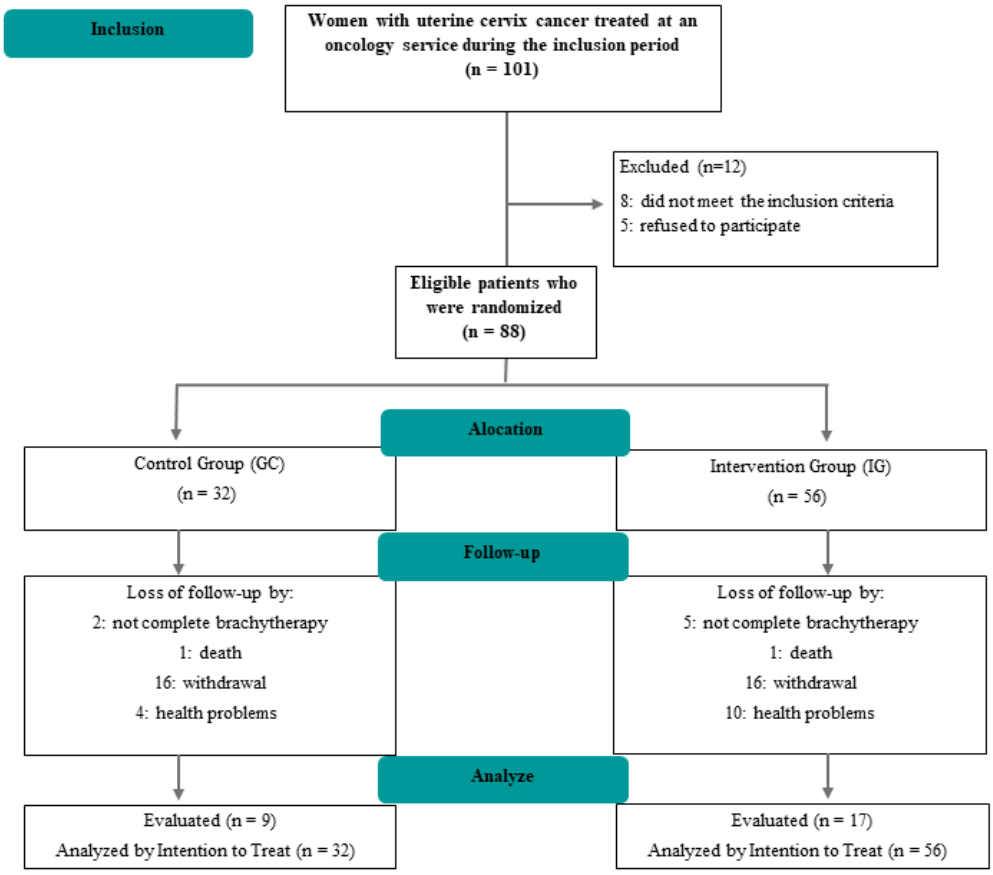



Figure 1

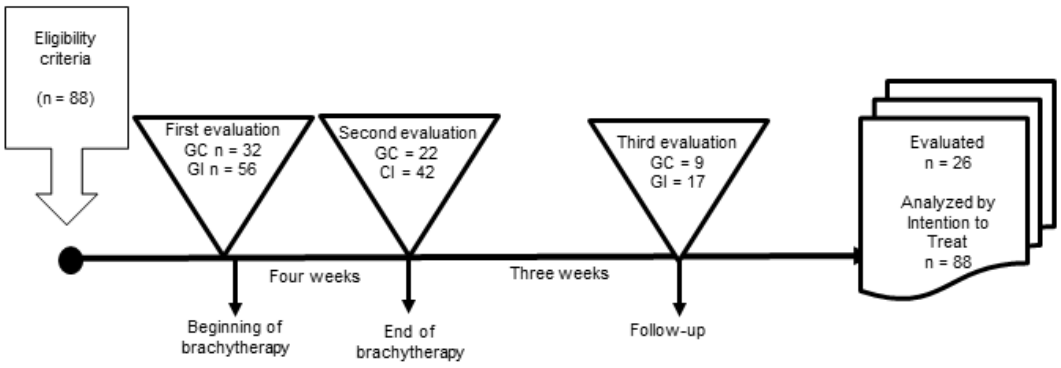



Figure 2

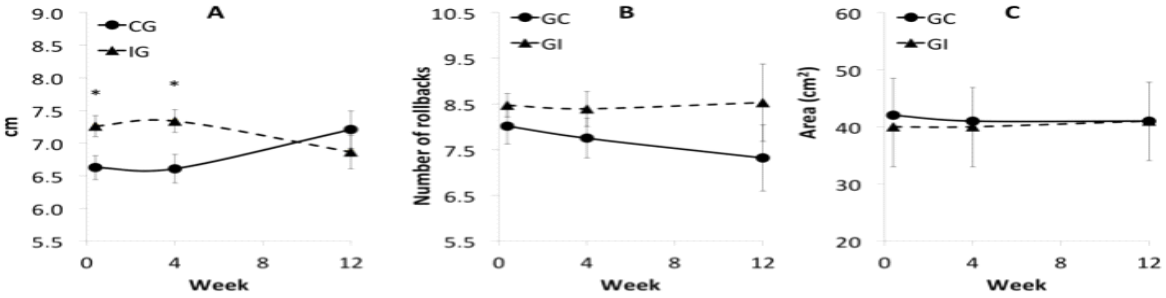

A
CG
IG
cm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
0
4
8
12
Week
B
GC
GI
Number of rollbacks
10.5
9.5
8.5
7.5
6.5
5.5
0
4
8
12
Week
C
GC
GI
Area (cm²)
60
50
40
30
20
0
4
8
12
Week

Figura 3

## 5 CONCLUSÃO GERAL

Esta revisão da literatura, aponta muitas fragilidades metodológicas nos estudos que utilizam a dilatação vaginal para a prevenção e/ou tratamento de alterações nas dimensões do canal vaginal de mulheres tratadas com RT, especialmente braquiterapia, para o câncer do colo do útero. Um problema evidente é a dificuldade de adesão desta população à programas de prevenção e acompanhamento, uma vez que as taxas de perdas para este tipo de proposta são bastante altas. Deve-se considerar que, talvez, neste momento mais precoce, o dano psicológico a estas mulheres seja maior, e mais importante, que o dano físico e portanto, deve receber maior atenção.

# ANEXOS

## ANEXO A

## Normas de formatação para a revista Archives of Gynecology and Obstetrics

**Manuscript Submission**

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

**Permissions**

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

**Online Submission**

Please follow the hyperlink “Submit online” on the right and upload all of your manuscript files following the instructions given on the screen.

**ORCID ID**

This publication requires that the corresponding author provides his/her ORCiD ID before proceeding with submission.

For more information about this journal’s ORCiD policy, please visit the ORCID FAQ

**Title Page**

The title page should include:

The name(s) of the author(s)

A concise and informative title

The affiliation(s) and address(es) of the author(s)

The e-mail address, and telephone number(s) of the corresponding author

If available, the 16-digit ORCID of the author(s)

**Abstract**

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:

Purpose (stating the main purposes and research question)

Methods

Results

Conclusions

**Keywords**

Please provide 4 to 6 keywords which can be used for indexing purposes.

**TEXT FORMATTING**

Manuscripts should be submitted in Word.

Use a normal, plain font (e.g., 10-point Times Roman) for text.

Use italics for emphasis.

Use the automatic page numbering function to number the pages.

Do not use field functions.

Use tab stops or other commands for indents, not the space bar.

Use the table function, not spreadsheets, to make tables.

Use the equation editor or MathType for equations.

Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

**Manuscripts with mathematical content can also be submitted in LaTeX.**

LaTeX macro package (zip, 182 kB)

**Headings**

Please use no more than three levels of displayed headings.

**Abbreviations**

Abbreviations should be defined at first mention and used consistently thereafter.

**Footnotes**

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

**Acknowledgments**

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

**REFERENCES**

**Citation**

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].

2. This result was later contradicted by Becker and Seligman [5].

3. This effect has been widely studied [1-3, 7].

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list.

The entries in the list should be numbered consecutively.

**Journal article**

Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. Eur J Appl Physiol 105:731-738. https://doi.org/10.1007/s00421-008-0955-8

Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:

Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. N Engl J Med 965:325–329

**Article by DOI**

Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. J Mol Med. https://doi.org/10.1007/s001090000086

**Book**

South J, Blass B (2001) The future of modern genomics. Blackwell, London

**Book chapter**

Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257

**Online document**

Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. http://physicsweb.org/articles/news/11/6/16/1. Accessed 26 June 2007

**Dissertation**

Trent JW (1975) Experimental acute renal failure. Dissertation, University of California

Always use the standard abbreviation of a journal's name according to the ISSN List of Title Word Abbreviations, see ISSN.org LTWA

**TABLES**

All tables are to be numbered using Arabic numerals.

Tables should always be cited in text in consecutive numerical order.

For each table, please supply a table caption (title) explaining the components of the table.

Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.

Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

**ARTWORK AND ILLUSTRATIONS GUIDELINES**

**Electronic Figure Submission**

Supply all figures electronically.

Indicate what graphics program was used to create the artwork.

For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.

Vector graphics containing fonts must have the fonts embedded in the files.

Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

Definition: Black and white graphic with no shading.

Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.

All lines should be at least 0.1 mm (0.3 pt) wide.

Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi.

Vector graphics containing fonts must have the fonts embedded in the files.

**Halftone Art**

halftone-gray-color

Definition: Photographs, drawings, or paintings with fine shading, etc.

If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.

Halftones should have a minimum resolution of 300 dpi.

Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.

Combination artwork should have a minimum resolution of 600 dpi.

**Color Art**

Color art is free of charge for online publication.

If black and white will be shown in the print version, make sure that the main information will still be visible. Many colors are not distinguishable from one another when converted to black and white. A simple way to check this is to make a xerographic copy to see if the necessary distinctions between the different colors are still apparent.

If the figures will be printed in black and white, do not refer to color in the captions.

Color illustrations should be submitted as RGB (8 bits per channel).

**Figure Lettering**

To add lettering, it is best to use Helvetica or Arial (sans serif fonts).

Keep lettering consistently sized throughout your final-sized artwork, usually about 2–3 mm (8–12 pt).

Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.

Avoid effects such as shading, outline letters, etc.

Do not include titles or captions within your illustrations.

**Figure Numbering**

All figures are to be numbered using Arabic numerals.

Figures should always be cited in text in consecutive numerical order.

Figure parts should be denoted by lowercase letters (a, b, c, etc.).

If an appendix appears in your article and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures,

"A1, A2, A3, etc." Figures in online appendices (Electronic Supplementary Material) should, however, be numbered separately.

**Figure Captions**

Each figure should have a concise caption describing accurately what the figure depicts. Include the captions in the text file of the manuscript, not in the figure file.

Figure captions begin with the term Fig. in bold type, followed by the figure number, also in bold type.

No punctuation is to be included after the number, nor is any punctuation to be placed at the end of the caption.

Identify all elements found in the figure in the figure caption; and use boxes, circles, etc., as coordinate points in graphs.

Identify previously published material by giving the original source in the form of a reference citation at the end of the figure caption.

**Figure Placement and Size**

Figures should be submitted separately from the text, if possible.

When preparing your figures, size figures to fit in the column width.

For most journals the figures should be 39 mm, 84 mm, 129 mm, or 174 mm wide and not higher than 234 mm.

For books and book-sized journals, the figures should be 80 mm or 122 mm wide and not higher than 198 mm.

**Permissions**

If you include figures that have already been published elsewhere, you must obtain permission from the copyright owner(s) for both the print and online format. Please be aware that some publishers do not grant electronic rights for free and that Springer will not be able to refund any costs that may have occurred to receive these permissions. In such cases, material from other sources should be used.

**Accessibility**

In order to give people of all abilities and disabilities access to the content of your figures, please make sure that

All figures have descriptive captions (blind users could then use a text-to-speech software or a text-to-Braille hardware)

Patterns are used instead of or in addition to colors for conveying information (colorblind users would then be able to distinguish the visual elements)

Any figure lettering has a contrast ratio of at least 4.5:1

**ELECTRONIC SUPPLEMENTARY MATERIAL**

Springer accepts electronic multimedia files (animations, movies, audio, etc.) and other supplementary files to be published online along with an article or a book chapter. This feature can add dimension to the author's article, as certain information cannot be printed or is more convenient in electronic form.

Before submitting research datasets as electronic supplementary material, authors should read the journal's Research data policy. We encourage research data to be archived in data repositories wherever possible.

**Submission**

Supply all supplementary material in standard file formats.

Please include in each file the following information: article title, journal name, author names; affiliation and e-mail address of the corresponding author.

To accommodate user downloads, please keep in mind that larger-sized files may require very long download times and that some users may experience other problems during downloading.

**Audio, Video, and Animations**

Aspect ratio: 16:9 or 4:3

Maximum file size: 25 GB

Minimum video duration: 1 sec

Supported file formats: avi, wmv, mp4, mov, m2p, mp2, mpg, mpeg, flv, mxf, mts, m4v, 3gp

**Text and Presentations**

Submit your material in PDF format; .doc or .ppt files are not suitable for long-term viability.

A collection of figures may also be combined in a PDF file.

**Spreadsheets**

Spreadsheets should be submitted as .csv or .xlsx files (MS Excel).

**Specialized Formats**

Specialized format such as .pdb (chemical), .wrl (VRML), .nb (Mathematica notebook), and .tex can also be supplied.

**Collecting Multiple Files**

It is possible to collect multiple files in a .zip or .gz file.

**Numbering**

If supplying any supplementary material, the text must make specific mention of the material as a citation, similar to that of figures and tables.

Refer to the supplementary files as “Online Resource”, e.g., "... as shown in the animation (Online Resource 3)", “... additional data are given in Online Resource 4”.

Name the files consecutively, e.g. “ESM_3.mpg”, “ESM_4.pdf”.

**Captions**

For each supplementary material, please supply a concise caption describing the content of the file.

Processing of supplementary files

Electronic supplementary material will be published as received from the author without any conversion, editing, or reformatting.

**Accessibility**

In order to give people of all abilities and disabilities access to the content of your supplementary files, please make sure that

The manuscript contains a descriptive caption for each supplementary material

Video files do not contain anything that flashes more than three times per second (so that users prone to seizures caused by such effects are not put at risk)

**ETHICAL RESPONSIBILITIES OF AUTHORS**

This journal is committed to upholding the integrity of the scientific record. As a member of the Committee on Publication Ethics (COPE) the journal will follow the COPE guidelines on how to deal with potential acts of misconduct.

Authors should refrain from misrepresenting research results which could damage the trust in the journal, the professionalism of scientific authorship, and ultimately the entire scientific endeavour.

Maintaining integrity of the research and its presentation can be achieved by following the rules of good scientific practice, which include:

The manuscript has not been submitted to more than one journal for simultaneous consideration.

The manuscript has not been published previously (partly or in full), unless the new work concerns an expansion of previous work (please provide transparency on the re-use of material to avoid the hint of text-recycling ("self-plagiarism")).

A single study is not split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (e.g. "salami-publishing").

No data have been fabricated or manipulated (including images) to support your conclusions

No data, text, or theories by others are presented as if they were the author's own ("plagiarism").

Proper acknowledgements to other works must be given (this includes material that is closely copied (near verbatim), summarized and/or paraphrased), quotation marks are used for verbatim copying of material, and permissions are secured for material that is copyrighted.

Important note: the journal may use software to screen for plagiarism.

Consent to submit has been received explicitly from all co-authors, as well as from the responsible authorities - tacitly or explicitly - at the institute/organization where the work has been carried out, before the work is submitted.

Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

Authors are strongly advised to ensure the correct author group, corresponding author, and order of authors at submission. Changes of authorship or in the order of authors are not accepted after acceptance of a manuscript.

Adding and/or deleting authors and/or changing the order of authors at revision stage may be justifiably warranted. A letter must accompany the revised manuscript to explain the reason for the change(s) and the contribution role(s) of the added and/or deleted author(s). Further documentation may be required to support your request.

Requests for addition or removal of authors as a result of authorship disputes after acceptance are honored after formal notification by the institute or independent body and/or when there is agreement between all authors.

Upon request authors should be prepared to send relevant documentation or data in order to verify the validity of the results. This could be in the form of raw data, samples, records, etc. Sensitive information in the form of confidential proprietary data is excluded.

If there is a suspicion of misconduct, the journal will carry out an investigation following the COPE guidelines. If, after investigation, the allegation seems to raise valid concerns, the accused author will be contacted and given an opportunity to address the issue. If misconduct has been

established beyond reasonable doubt, this may result in the Editor-in-Chief's implementation of the following measures, including, but not limited to:

If the article is still under consideration, it may be rejected and returned to the author.

If the article has already been published online, depending on the nature and severity of the infraction, either an erratum will be placed with the article or in severe cases complete retraction of the article will occur. The reason must be given in the published erratum or retraction note. Please note that retraction means that the paper is maintained on the platform, watermarked "retracted" and explanation for the retraction is provided in a note linked to the watermarked article.

The author's institution may be informed.

**COMPLIANCE WITH ETHICAL STANDARDS**

To ensure objectivity and transparency in research and to ensure that accepted principles of ethical and professional conduct have been followed, authors should include information regarding sources of funding, potential conflicts of interest (financial or non-financial), informed consent if the research involved human participants, and a statement on welfare of animals if the research involved animals.

Authors should include the following statements (if applicable) in a separate section entitled "Compliance with Ethical Standards" when submitting a paper:

Disclosure of potential conflicts of interest

Research involving Human Participants and/or Animals

**Informed consent**

Please note that standards could vary slightly per journal dependent on their peer review policies (i.e. single or double blind peer review) as well as per journal subject discipline. Before submitting your article check the instructions following this section carefully.

The corresponding author should be prepared to collect documentation of compliance with ethical standards and send if requested during peer review or after publication.

The Editors reserve the right to reject manuscripts that do not comply with the above-mentioned guidelines. The author will be held responsible for false statements or failure to fulfill the above-mentioned guidelines.

**DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST**

Authors must disclose all relationships or interests that could have direct or potential influence or impart bias on the work. Although an author may not feel there is any conflict, disclosure of

relationships and interests provides a more complete and transparent process, leading to an accurate and objective assessment of the work. Awareness of a real or perceived conflicts of interest is a perspective to which the readers are entitled. This is not meant to imply that a financial relationship with an organization that sponsored the research or compensation received for consultancy work is inappropriate. Examples of potential conflicts of interests that are directly or indirectly related to the research may include but are not limited to the following:

Research grants from funding agencies (please give the research funder and the grant number)

Honoraria for speaking at symposia

Financial support for attending symposia

Financial support for educational programs

Employment or consultation

Support from a project sponsor

Position on advisory board or board of directors or other type of management relationships

Multiple affiliations

Financial relationships, for example equity ownership or investment interest

Intellectual property rights (e.g. patents, copyrights and royalties from such rights)

Holdings of spouse and/or children that may have financial interest in the work

In addition, interests that go beyond financial interests and compensation (non-financial interests) that may be important to readers should be disclosed. These may include but are not limited to personal relationships or competing interests directly or indirectly tied to this research, or professional interests or personal beliefs that may influence your research.

The corresponding author collects the conflict of interest disclosure forms from all authors. In author collaborations where formal agreements for representation allow it, it is sufficient for the corresponding author to sign the disclosure form on behalf of all authors

The corresponding author will include a summary statement in the text of the manuscript in a separate section before the reference list, that reflects what is recorded in the potential conflict of interest disclosure form(s).

Please make sure to submit all Conflict of Interest disclosure forms together with the manuscript.

See below examples of disclosures:

Funding: This study was funded by X (grant number X).

Conflict of Interest: Author A has received research grants from Company A. Author B has received a speaker honorarium from Company X and owns stock in Company Y. Author C is a member of committee Z.

If no conflict exists, the authors should state:

Conflict of Interest: The authors declare that they have no conflict of interest.

**RESEARCH INVOLVING HUMAN PARTICIPANTS AND/OR ANIMALS**

1) Statement of human rights

When reporting studies that involve human participants, authors should include a statement that the studies have been approved by the appropriate institutional and/or national research ethics committee and have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

If doubt exists whether the research was conducted in accordance with the 1964 Helsinki Declaration or comparable standards, the authors must explain the reasons for their approach, and demonstrate that the independent ethics committee or institutional review board explicitly approved the doubtful aspects of the study.

The following statements should be included in the text before the References section:

Ethical approval: "All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

For retrospective studies, please add the following sentence:

"For this type of study formal consent is not required."

2) Statement on the welfare of animals

The welfare of animals used for research must be respected. When reporting experiments on animals, authors should indicate whether the international, national, and/or institutional guidelines for the care and use of animals have been followed, and that the studies have been approved by a research ethics committee at the institution or practice at which the studies were conducted (where such a committee exists).

For studies with animals, the following statement should be included in the text before the References section:

Ethical approval: "All applicable international, national, and/or institutional guidelines for the care and use of animals were followed."

If applicable (where such a committee exists): “All procedures performed in studies involving animals were in accordance with the ethical standards of the institution or practice at which the studies were conducted.”

If articles do not contain studies with human participants or animals by any of the authors, please select one of the following statements:

“This article does not contain any studies with human participants performed by any of the authors.”

“This article does not contain any studies with animals performed by any of the authors.”

“This article does not contain any studies with human participants or animals performed by any

**INFORMED CONSENT**

All individuals have individual rights that are not to be infringed. Individual participants in studies have, for example, the right to decide what happens to the (identifiable) personal data gathered, to what they have said during a study or an interview, as well as to any photograph that was taken. Hence it is important that all participants gave their informed consent in writing prior to inclusion in the study. Identifying details (names, dates of birth, identity numbers and other information) of the participants that were studied should not be published in written descriptions, photographs, and genetic profiles unless the information is essential for scientific purposes and the participant (or parent or guardian if the participant is incapable) gave written informed consent for publication. Complete anonymity is difficult to achieve in some cases, and informed consent should be obtained if there is any doubt. For example, masking the eye region in photographs of participants is inadequate protection of anonymity. If identifying characteristics are altered to protect anonymity, such as in genetic profiles, authors should provide assurance that alterations do not distort scientific meaning.

The following statement should be included:

Informed consent: “Informed consent was obtained from all individual participants included in the study.”

If identifying information about participants is available in the article, the following statement should be included:

“Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.” of the authors.”

**ENGLISH LANGUAGE EDITING**

For editors and reviewers to accurately assess the work presented in your manuscript you need to ensure the English language is of sufficient quality to be understood. If you need help with writing in English you should consider:

Asking a colleague who is a native English speaker to review your manuscript for clarity.

Visiting the English language tutorial which covers the common mistakes when writing in English.

Using a professional language editing service where editors will improve the English to ensure that your meaning is clear and identify problems that require your review. Two such services are provided by our affiliates Nature Research Editing Service and American Journal Experts. Springer authors are entitled to a 10% discount on their first submission to either of these services, simply follow the links below.

English language tutorial

Nature Research Editing Service

American Journal Experts

Please note that the use of a language editing service is not a requirement for publication in this journal and does not imply or guarantee that the article will be selected for peer review or accepted.

If your manuscript is accepted it will be checked by our copyeditors for spelling and formal style before publication.

**RESEARCH DATA POLICY**

Support for Research Data Sharing

Many journals and funding agencies encourage or require data sharing in repositories. If you need help organising and sharing your research data (including code, text, raw and processed data, video and images) you should consider:

Finding a suitable data repository for your data

Uploading your data to Springer Nature Research Data Support

Contacting Springer Nature's Research Data Support Helpdesk for advice

List of recommended data repositories

Access Research Data Support

More information on Research Data Support

Contact the Research Data Helpdesk

Research Data Support is an optional Springer Nature service available to all researchers who have datasets they want to make easier to cite, share and find. The service provides a secure portal for

data upload, and data and metadata are curated and improved by professional Research Data Editors. The publication of datasets is coordinated by our Research Data Editors in consultation with the researcher, and a DOI is provided to allow the dataset to be cited and shared.

Checks are carried out as part of a submission screening process to ensure that researchers who should use a specific community-endorsed repository are advised of the best option for sharing and archiving their data. Use of Research Data Support is optional and does not imply or guarantee that a manuscript will be accepted.

# ANEXO B

## Parecer do Comitê de Ética em Pesquisa

IRMANDADE DA SANTA CASA DE MISERICORDIA DE PORTO ALEGRE - ISCMPA

**PARECER CONSUBSTANCIADO DO CEP**

**DADOS DO PROJETO DE PESQUISA**

**Título da Pesquisa:** Fisioterapia pélvica na prevenção da estenose vaginal secundária ao tratamento radioterápico do câncer ginecológico.

**Pesquisador:** Fabricio Edler Macagnan

**Área Temática:**

**Versão:** 2

**CAAE:** 63083516.4.0000.5335

**Instituição Proponente:** Irmandade da Santa Casa de Misericordia de Porto Alegre - ISCMPA

**Patrocinador Principal:** Financiamento Próprio

**DADOS DO PARECER**

**Número do Parecer:** 2.017.148

**Apresentação do Projeto:**

A estenose vaginal é um dos efeitos secundários mais prevalentes a radiação pélvica, afetando cerca de um terço das mulheres. Objetivo: avaliar o efeito de um protocolo de fisioterapia pélvica sobre a taxa de incidência de estenose vaginal após o tratamento do câncer ginecológico por radioterapia que utilize o modo de braquiterapia pélvica. Métodos: Será realizado um ensaio clínico randomizado e controlado, com 160 pacientes, que foram encaminhadas para braquiterapia pélvica no Hospital Santa Rita – Complexo Santa Casa de Misericórdia de Porto Alegre. O desfecho primário será a possibilidade de a fisioterapia pélvica alterar ou não a incidência de estenose vaginal em mulheres submetidas a braquiterapia pélvica. Os desfechos secundários serão os efeitos da fisioterapia pélvica sobre a qualidade de vida, sexualidade e função contrátil dos músculos do assoalho pélvico de mulheres com câncer ginecológico submetidas ao tratamento radioterápico. As pacientes serão alocadas em dois grupos aleatoriamente onde passarão por uma avaliação pré-braquiterapia e reavaliação após o termino das quatro sessões de braquiterapia e três e seis meses após o termino das sessões de braquiterapia. Serão realizadas a avaliação cinesiológico-funcional da musculatura do assoalho pélvico, eletromiografia dos músculos do assolho pélvico, medida da área vaginal através dos dilatadores. O comprimento da vagina será medido com um histerômetro. O grupo controle não receberá nenhuma intervenção da

**Endereço:** R. Profº Annes Dias,295 Hosp.Dom Vicente Scherer
**Bairro:** 6º andar - Centro **CEP:** 90.020-090
**UF:** RS **Município:** PORTO ALEGRE
**Telefone:** (51)3214-8571 **Fax:** (51)3214-8571 **E-mail:** cep@santacasa.tche.br




fisioterapia, somente as orientações habituais do serviço. O grupo intervenção realizará um protocolo com exercícios para o assolho pélvico e uso de dilatadores vaginais.

**Objetivo da Pesquisa:**

Objetivo Primário:

Avaliar o efeito de um protocolo de fisioterapia pélvica sobre a taxa de incidência de estenose vaginal em curto e médio prazo após a braquiterapia pélvica no tratamento do câncer ginecológico.

Objetivo Secundário:

Avaliar o efeito de um protocolo de fisioterapia pélvica sobre:a) Incidência de estenose vaginal ao final do período de braquiterapia pélvica;b) Incidência de estenose vaginal após três meses do término da braquiterapia pélvica;c) Incidência de estenose vaginal após seis meses do término da braquiterapia pélvica;d) Qualidade de vida ao longo dos quatro momentos de avaliação;e) Sexualidade ao longo dos quatro momentos de avaliação;f) Contratilidade dos músculos do assoalho pélvico ao longo dos quatro momentos de avaliação.

**Avaliação dos Riscos e Benefícios:**

Riscos:

O protocolo poderá não trazer benefícios quanto a prevenção da estenose vaginal secundária a braquiterapia. Após as sessões de fisioterapia onde serão realizados procedimentos intracavitários, é possível que a sensação de desconforto e até mesmo pequenos sangramentos ocorram ao utilizar os dilatadores vaginais. É importante ressaltar que desconforto e pequenos sangramentos são situações clínicas previstas no tratamento de braquiterapia ginecológica convencional, e que o atendimento a estas situações é realizado pela própria equipe multiprofissional do serviço de Radioterapia onde este estudo está sendo desenvolvido. As avaliações e os atendimentos fisioterapêuticos previstos nesta pesquisa serão realizados dentro do ambiente do serviço de Radioterapia em horários e dias em que a equipe desenvolve a rotina dos atendimentos às pacientes em tratamento com braquiterapia ginecológica. Por isso, se houver qualquer dificuldade em seguir com as avaliações ou mesmo durantes os atendimentos fisioterapêuticos, independentemente do motivo, a paciente poderá solicitar avaliação e atendimento à equipe de pesquisa que estará lhe atendendo, ou através do contato telefônico com pesquisador responsável conforme informado no TCLE.




Benefícios:

A paciente será submetida a atendimentos de fisioterapia pélvica que visam prevenir ou minimizar a ocorrência de estenose vaginal que muitas vezes ocorre após a braquiterapia, além de fortalecer os músculos do assoalho pélvico, evitando fraqueza muscular e consequentemente incrementando sua satisfação sexual e melhorando sua qualidade de vida.

**Comentários e Considerações sobre a Pesquisa:**

Após deliberações do CEP - Comitê de Ética em Pesquisa constatamos não haver óbice para a continuidade deste estudo.

**Considerações sobre os Termos de apresentação obrigatória:**

Foram apresentados os termos obrigatórios a este Comitê.

**Recomendações:**

Não há recomendações.

**Conclusões ou Pendências e Lista de Inadequações:**

Após deliberações do CEP - Comitê de Ética em Pesquisa constatamos não haver óbice para a continuidade deste estudo.

**Considerações Finais a critério do CEP:**

Após reavaliação do protocolo acima descrito, o presente comitê não encontrou óbices quanto ao desenvolvimento do estudo em nossa Instituição, o centro responsável pela submissão do projeto na Plataforma Brasil será o nosso CEP da Irmandade da Santa Casa de Misericórdia de Porto Alegre – RS.

**Este parecer foi elaborado baseado nos documentos abaixo relacionados:**

| Tipo Documento | Arquivo | Postagem | Autor | Situação |
|---|---|---|---|---|
| Informações Básicas do Projeto | PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_831736.pdf | 11/03/2017 14:02:07 | | Aceito |
| Outros | carta_ao_CEP_ISCMPA.pdf | 11/03/2017 14:01:18 | Taís Marques Cerentini | Aceito |
| TCLE / Termos de Assentimento / Justificativa de Ausência | TCLE_versao2_2017.pdf | 09/03/2017 12:31:16 | Taís Marques Cerentini | Aceito |
| Cronograma | cronograma_versao_2_final.pdf | 08/03/2017 14:16:47 | Taís Marques Cerentini | Aceito |

**Endereço:** R. Profº Annes Dias,295 Hosp.Dom Vicente Scherer
**Bairro:** 6º andar - Centro **CEP:** 90.020-090
**UF:** RS **Município:** PORTO ALEGRE
**Telefone:** (51)3214-8571 **Fax:** (51)3214-8571 **E-mail:** cep@santacasa.tche.br

| | | | | |
|---|---|---|---|---|
| Outros | Termo_anuencia_diretor_medico_HSR.pdf | 09/12/2016 13:47:32 | Taís Marques Cerentini | Aceito |
| Outros | Declaracao_autorizacao_diretor_medico_HSR.pdf | 09/12/2016 13:46:30 | Taís Marques Cerentini | Aceito |
| Outros | Termo_anuencia_coordenador_medico_radioterapia_HSR.jpg | 09/12/2016 13:45:55 | Taís Marques Cerentini | Aceito |
| Outros | Declaracao_autorizacao_Coordenador_medico_Radioterapia_HSR.jpg | 09/12/2016 13:44:49 | Taís Marques Cerentini | Aceito |
| Outros | Termo_anuencia_instituicao_chefe_fisioterapia_HSR.jpg | 09/12/2016 13:42:06 | Taís Marques Cerentini | Aceito |
| Outros | Declaracao_autorizacao_chefia_servico_fisioterapia_HSR.jpg | 09/12/2016 13:41:08 | Taís Marques Cerentini | Aceito |
| Outros | Termo_de_compromisso_para_entrega_de_relatorio_final_ou_semestral.jpg | 07/12/2016 23:16:34 | Taís Marques Cerentini | Aceito |
| Outros | Formulario_de_inscricao_de_projetos_de_pesquisa_CEP_ISCMPA.jpg | 07/12/2016 23:14:58 | Taís Marques Cerentini | Aceito |
| Outros | Declaracao_de_utilizacao_de_dados_de_prontuarios_e_uso_de_publicacao.jpg | 07/12/2016 23:13:39 | Taís Marques Cerentini | Aceito |
| Outros | Declaracao_de_confidencialidade_de_sujeitos_do_Estudo.jpg | 07/12/2016 23:12:56 | Taís Marques Cerentini | Aceito |
| Outros | Declaracao_de_isencao_de_onus_a_instituicao.jpg | 07/12/2016 23:12:24 | Taís Marques Cerentini | Aceito |
| Projeto Detalhado / Brochura Investigador | PROJETOFINAL.pdf | 07/12/2016 23:05:55 | Taís Marques Cerentini | Aceito |
| Orçamento | orcamento.pdf | 07/12/2016 22:48:24 | Taís Marques Cerentini | Aceito |
| Declaração de Manuseio Material Biológico / Biorepositório / Biobanco | declaracao_mat_biolo.jpg | 07/12/2016 22:46:57 | Taís Marques Cerentini | Aceito |
| Folha de Rosto | folhaderosto.pdf | 07/12/2016 19:11:40 | Taís Marques Cerentini | Aceito |

**Situação do Parecer:**
Aprovado

**Necessita Apreciação da CONEP:**
Não




PORTO ALEGRE, 17 de Abril de 2017

**Assinado por:**
**ELIZETE KEITEL**
**(Coordenador)**

**Endereço:** R. Profº Annes Dias,295 Hosp.Dom Vicente Scherer
**Bairro:** 6º andar - Centro **CEP:** 90.020-090
**UF:** RS **Município:** PORTO ALEGRE
**Telefone:** (51)3214-8571 **Fax:** (51)3214-8571 **E-mail:** cep@santacasa.tche.br