



HAL
open science

Terminology for cone dimensions after local conservative treatment for cervical intraepithelial neoplasia and early invasive cervical cancer: 2022 consensus recommendations from ESGO, EFC, IFCPC, and ESP

Maria Kyrgiou, Antonios Athanasiou, Marc Arbyn, Sigurd Lax, Maria Rosaria Raspollini, Pekka Nieminen, Xavier Carcopino, Jacob Bornstein, Murat Gultekin, Evangelos Paraskevaidis

► **To cite this version:**

Maria Kyrgiou, Antonios Athanasiou, Marc Arbyn, Sigurd Lax, Maria Rosaria Raspollini, et al.. Terminology for cone dimensions after local conservative treatment for cervical intraepithelial neoplasia and early invasive cervical cancer: 2022 consensus recommendations from ESGO, EFC, IFCPC, and ESP. *Lancet Oncology*, 2022, 23 (8), pp.e385-e392. 10.1016/S1470-2045(22)00191-7 . hal-03931291

HAL Id: hal-03931291

<https://hal.science/hal-03931291v1>

Submitted on 9 Jan 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Terminology for cone dimensions after local conservative treatment for cervical intraepithelial neoplasia and early invasive cervical cancer: 2022 consensus recommendations from ESGO, EFC, IFCCP, and ESP

Maria Kyrgiou, Antonios Athanasiou, Marc Arbyn, Sigurd F Lax, Maria Rosaria Raspollini, Pekka Nieminen, Xavier Carcopino, Jacob Bornstein, Murat Gultekin, Evangelos Paraskevaïdis

Local cervical treatment for squamous intraepithelial lesion (SIL) or cervical intraepithelial neoplasia (CIN) removes or ablates a cone-shaped or dome-shaped part of the cervix that contains abnormal cells. This Series paper introduces the 2022 terminology for cone dimensions after local conservative treatment for SIL, CIN, or early invasive cervical cancer. The terminology was prepared by the Nomenclature Committee of the European Society of Gynaecologic Oncology, the European Federation for Colposcopy, the International Federation of Cervical Pathology and Colposcopy, and the European Society of Pathology. Cone length should be tailored to the type of transformation zone. Treatment of SIL or CIN is associated with an increased risk of preterm birth, which escalates with increasing cone length. There is a lack of agreement regarding terms used to report excised specimen dimensions both intraoperatively and in the pathology laboratory. Consensus is needed to make studies addressing effectiveness and safety of SIL or CIN treatment comparable, and to facilitate their use to improve accuracy of antenatal surveillance and management. This Series paper summarises the current terminology through a review of existing literature, describes new terminology as agreed by a group of experts from international societies in the field of cervical cancer prevention and treatment, and recommends use of the new terminology that will facilitate communication between clinicians and foster more specific treatment guidelines that balance obstetrical harm against therapeutic effectiveness.

Introduction

Cervical cancer can be prevented by local treatment of screen-detected precursors, such as high-grade squamous intraepithelial lesions—also known as cervical intraepithelial neoplasia (CIN) of grade 2 or worse (CIN2+).^{1–3} In England, almost 5 million women are invited for cervical cancer screening and more than 33 000 cervical high-grade abnormalities are diagnosed each year,⁴ although this figure is expected to substantially reduce with the advent of vaccination.⁵

Local cervical treatment for squamous intraepithelial lesion (SIL) or CIN removes or ablates a cone-shaped or dome-shaped part of the cervix that contains abnormal cells. Nowadays, excisional treatments are preferred over ablation⁶ because they permit histological exploration of excised tissue to rule out invasion and assess for the presence of residual disease at the excision margins. Large loop excision of the transformation zone (LLETZ), also known as loop electrosurgical excisional procedure, is the treatment of choice in most European countries because of the ease and speed of execution, rapid learning curve, and low cost (figure 1). However, preferred treatment varies throughout Europe and globally, with some countries regularly offering cold knife conisation (CKC), laser conisation, needle excision of the transformation zone, or types of ablation.⁹

Complications of surgical conservative treatments were thought to be relatively mild and infrequent and

were historically described as primary or secondary haemorrhage, infection, and cervical stenosis. However, evidence published in the past 15 years has also associated these procedures with increased reproductive morbidity in women who become pregnant after treatment.^{10–14} The extent of the risk of reproductive morbidity appears to be directly correlated to the dimensions of the cone removed.^{13–17} The length of the excised specimen (cone) is commonly used to inform women about their individual risk, and to make antenatal surveillance and interventions more accurate and effective in subsequent pregnancies. Cone length has also been correlated with disease recurrence rates (eg, the smaller the cone, the higher the recurrence rate).¹⁸

Although the size of the excised specimen is widely used by gynaecologists and pathologists to counsel women and assess treatment, there is a lack of consensus regarding the nomenclature describing dimensions of excised specimens and principles of reporting before and after formalin fixation. Different terminology has been adopted by various gynaecological¹⁹ and pathological²⁰ societies, with little interaction between the two groups. In this Series paper, we synthesise existing literature about historically used terminology by gynaecological societies in the clinic at the time of treatment, and by pathological societies in the histopathology laboratory. We discuss how the dimensions of excised specimens could be used to assist clinical decision making, and

Institute of Reproductive and Developmental Biology, Department of Metabolism, Digestion, and Reproduction (Prof M Kyrgiou PhD, A Athanasiou MBBSeq) and Department of Surgery and Cancer, Imperial College London, London, UK (Prof M Kyrgiou, A Athanasiou); Imperial College Healthcare NHS Trust, London, UK (Prof M Kyrgiou, A Athanasiou, Prof E Paraskevaïdis PhD); Unit of Cancer Epidemiology, Belgian Cancer Centre, Sciensano, Brussels, Belgium (Prof M Arbyn PhD); Department of Human Structure and Repair, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium (Prof M Arbyn); Department of Pathology, Hospital Graz II, Medical University of Graz, Graz, Austria (Prof S F Lax PhD); School of Medicine, Johannes Kepler University Linz, Linz, Austria (Prof S F Lax); Histopathology and Molecular Diagnostics, Careggi University Hospital, Florence, Italy (M R Raspollini PhD); Department of Obstetrics and Gynaecology, Helsinki University Central Hospital, Helsinki, Finland (P Nieminen PhD); Department of Obstetrics and Gynaecology, Hôpital Nord, APHM, Aix-Marseille University, Marseille, France (Prof X Carcopino PhD); Department of Obstetrics and Gynaecology, Galilee Medical Center, Nahariya, Israel (Prof J Bornstein MD); Department of Obstetrics and

Gynaecology, Azrieli Faculty of Medicine, Bar-Ilan University, Nahariya, Israel (Prof J Bornstein); Division of Gynaecological Oncology, Department of Obstetrics and Gynaecology, Hacettepe University Faculty of Medicine, Ankara, Türkiye (M Gultekin PhD); Department of Obstetrics and Gynaecology, University Hospital of Ioannina, Ioannina, Greece (Prof E Paraskevaidis)

Correspondence to: Prof Maria Kyrgiou, Institute of Reproductive and Developmental Biology, Department of Metabolism, Digestion, and Reproduction and Department of Surgery and Cancer, Imperial College London, London W12 0NN, UK
 m.kyrgiou@imperial.ac.uk

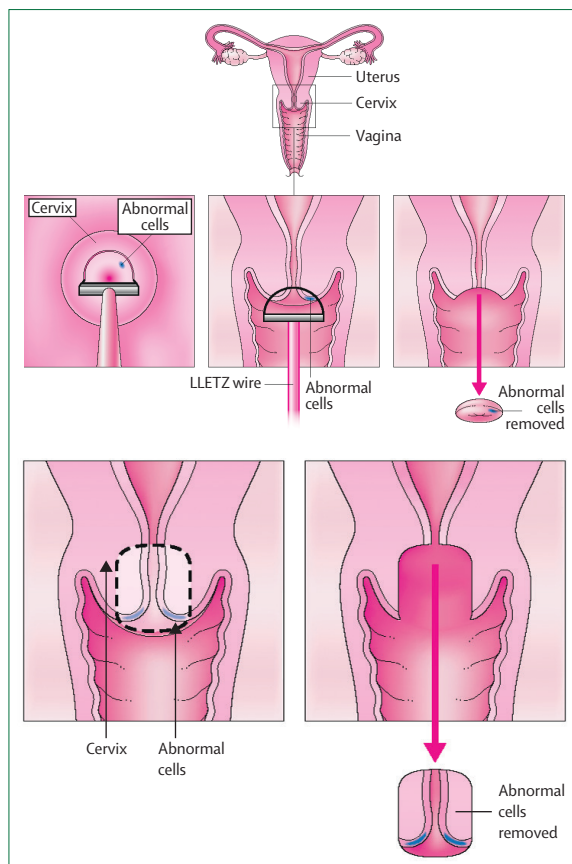


Figure 1: Local excision of the transformation zone
 Adapted with permission from Jo's Cervical Cancer Trust.⁷⁸ LLETZ=large loop excision of the transformation zone.

present joint nomenclature from the European Society of Gynaecologic Oncology (ESGO), the European Federation for Colposcopy (EFC), the International Federation of Cervical Pathology and Colposcopy (IFCPC), and the European Society of Pathology (ESP) for the description of these dimensions to be used in clinical reporting. Assessment of such reporting to date is hampered by the use of different terms across studies.

Oncological outcomes

Local treatment for SIL or CIN is highly efficacious in preventing cervical cancer and high-grade preinvasive lesion recurrence. Arbyn and colleagues²¹ reported an average risk of histologically confirmed high-grade lesion recurrence of only 6·6% following treatment.

Although a Cochrane review²² reported no evidence of a difference in risk of lesion recurrence between surgical techniques, this review only included small randomised controlled studies, so was underpowered to show significant differences between highly efficacious methods of treatment. Emerging data suggest that length and radicality of treatment might affect that risk.²³ In the meta-analysis by Arbyn and colleagues,²¹ LLETZ had a 6·7% risk of high-grade SIL or CIN recurrence, whereas

CKC and laser conisation only had a 2·1–2·2% risk of recurrence. Additionally, Strander and colleagues²⁴ reported a gradual increase in age-standardised incidence of invasive cervicovaginal cancer after excisional treatment over the span of five decades, which could partly be explained by the increasing use of less radical surgical techniques. Further research combining observational and randomised evidence is expected to clarify the efficacy of various treatments.²⁵

There is a small amount of evidence regarding the association between lesion recurrence rates and the dimensions of excised specimens. Bae and colleagues²⁶ in a 2013 Korean retrospective cohort study of 1220 women (289 women [24%] CIN grade 2 [CIN2], 916 women [75%] CIN grade 3 [CIN3], and 15 women [1%] stage 1a1 cervical cancer), suggested that cone length should be adjusted according to the age and grade of a lesion (<40 years and CIN2: ≥ 9 mm; 40–50 years and CIN2: ≥ 12 mm; <50 years and CIN3 or stage 1a1 cervical cancer: ≥ 18 mm). A cone length of at least 18 mm would be required to achieve resection of a clear endocervical margin in 86% of women younger than 50 years with CIN2+ and in 88% of women younger than 40 years with CIN2+. For CIN2, a 9 mm cone length achieved clearance in 83% of women younger than 50 years, whereas a cone length of 12 mm would be required to achieve clearance in 90% of women younger than 50 years.²⁶ An observational study by Ang and colleagues¹⁸ of 1558 treated women (482 [31%] CIN2, 1076 [69%] CIN3) found a significantly higher rate of involved endocervical margins in excised specimens measuring less than 10 mm in length than in larger excised specimens in both younger and older women (≤ 35 years, <10 mm vs ≥ 10 mm: 24% vs 13%, $p < 0\cdot001$; >35 years, <10 mm vs ≥ 10 mm: 41% vs 26%, $p = 0\cdot008$). However, the study reported that the difference in rates of margin clearance between specimen lengths led to an increased risk of CIN2+ recurrence for women older than 35 years (but not in younger women). Although margin status is associated with treatment failure, other evidence suggests that human papillomavirus (HPV) clearance is a better predictor of disease outcomes.²¹ No studies have explored the effect of cone length on lesion recurrence rates for glandular disease alone.

Reproductive outcomes

Local SIL or CIN treatment has been reported to increase the risk of adverse reproductive outcomes in subsequent pregnancies.^{23,27} In the UK, 2·5% of total preterm births each year (840 preterm births, including 196 with gestational age of <32 weeks) were attributed to previous treatment for SIL or CIN.²⁸ The first meta-analysis to recognise this association was published in 2006.¹⁰ It reported an increased risk of preterm birth, defined as birth at fewer than 37 weeks' gestation, after CKC (14%) versus no treatment (5%; relative risk 2·59, 95% CI 1·80–3·72) and LLETZ (11%) versus no treatment (7%;

1.70, 1.24–2.35). A subsequent meta-analysis of 20 studies was the first to report that the frequency and severity of reproductive complications increased when surgical treatment methods that are known to remove large amounts of cervical tissue were used.²⁹ Although SIL or CIN treatment has not been found to affect pregnancy rates, it has been associated with an increased risk of second-trimester miscarriage.^{11,12,30}

An update to Kyrgiou and colleagues¹⁰ was published in 2016 and was the first meta-analysis to report that excised specimen length, dimensions, and volume can stratify the rate of reproductive risk.¹³ This meta-analysis reported a relative increase in risk of preterm birth for women after any local treatment compared with no treatment of 1.54 (95% CI 1.09–2.18) for excised specimen lengths up to 10 mm, 1.93 (1.62–2.31) for those measuring 10–15 mm, 2.77 (1.95–3.93) for those measuring 15–20 mm, and 4.91 (2.06–11.68) for those measuring more than 20 mm. The meta-analysis also reported that having SIL or CIN conferred an increased risk of preterm birth, but local treatment increased this risk even further. The additional risk of preterm birth conferred by cones of less than 10 mm in length remains unclear. Noehr and colleagues³¹ reported a 6% increase in risk of preterm birth for every additional millimetre of cone length more than 12 mm. A case-control study by Castanon and colleagues,³² nested within a record linkage cohort study of 12 UK hospitals, reported that the absolute risks for preterm birth for small excisional treatments (<10 mm in length) was similar to that of a diagnostic punch biopsy only (7.5% vs 7.2%). However, the risk of preterm birth escalated with increasing length of excised specimen (9.6% for medium size excised specimens [10–14 mm], 15.3% for large size excised specimens [15–19 mm], and 18.0% for very large size excised specimens [>20 mm]). The authors also concluded that excised specimen volumes of more than 2.65 cm³ doubled the risk of preterm birth compared with excised specimen volumes of less than 2.65 cm³.³² Khalid and colleagues¹⁶ reported that risk of preterm birth increased by 150% when cone length exceeded 20 mm (compared with <10 mm), and increased by 300% when excised specimen volume was greater than 6 cm³ (compared with <3 cm³).¹⁶

Proportional length or volume of cervix removed might be a stronger predictor of poor reproductive outcomes than absolute length or volume of cervix removed, as pretreatment dimensions of a cervix can vary substantially.^{15,17} Research in network meta-analyses^{25,33,34} provided further evidence regarding how cone dimensions or treatment technique affect risk of recurrence or preterm birth.

Previous terminology

In the clinic or operating theatre

The practice of excised specimen measurement before formalin fixation has emerged since the awareness that

local SIL or CIN treatment increases the risk of preterm birth in subsequent pregnancies. It has been proposed that excised specimen measurement taken at the time of treatment prior to formalin fixation might be more accurate than excised specimen measurement taken in the histopathology laboratory after formalin fixation.³⁵ Cone size has been suggested as a useful measurement for risk stratification that could predict individualised risk of obstetrical complications and make antenatal surveillance and preventive interventions more accurate and effective. Historically, different metrics have been used to describe the dimensions of excised tissue specimens, although these metrics are not universally accepted.

Cone dimensions

The IFCPC attempted to standardise terminology for cone dimensions by publishing guidelines in 2012.¹⁹ The terminology in these guidelines is the same as the terminology published by Khalid and colleagues¹⁶ in 2012 (appendix pp 2–3, 5). The IFCPC recognised a lack of consensus in published literature regarding the terms used to describe cone dimensions. For example, the distance from the ectocervical margin to the endocervical margin has been variably reported as length, depth, or height in different publications. As a result, the IFCPC advised abandoning the terms depth and height, and proposed using the term length instead. Furthermore, they introduced the terms thickness and circumference to describe other relevant cone dimensions. However, despite their introduction, these terms have not been largely adopted in clinical practice because of challenges in measuring these dimensions and a lack of guidance regarding how these new terms can affect clinical decision making. Given the asymmetry of excision cones, for example, use of the term thickness (radius) varies in the four quadrants of a cone, and anteroposterior and transverse dimensions are suggested to be more representative of their true size.

Cone volume

Several approaches have been proposed for the measurement of cone volume. The volumetric fluid displacement technique is likely to represent the most accurate measurement (the gold standard), whereby the difference in fluid level before and after the immersion of a cone is recorded (Archimedes' principle; appendix p 6).^{15,17,36–42} When this technique is not feasible, researchers have used various formulas to calculate the volume of a cone from its dimensions.^{16,32,43–54} As the shape of cones can vary, researchers have used different cone shapes to determine volume, such as a cone, a semi-ellipsoid, an ellipsoid, a parallelepiped, and a truncated cone (frustum; appendix pp 2–3, 7–8).

Cervical dimensions

Cervical dimensions (anteroposterior dimension, transverse dimension, and length) have historically been

Definition	
Cone dimensions	
Length	Distance between the ectocervical (external or distal) and endocervical (internal or proximal) margin of the cone
Anteroposterior dimension	Distance between the anterior and posterior margin of the cone; if the cone is not oriented, the anteroposterior dimension should be randomly selected
Transverse dimension	Distance between the left and right margin of the cone; if the cone is not oriented, the transverse dimension should be randomly selected
Cone volume	
Fluid displacement technique	Volumetric tube
Formula	Semi-ellipsoid: $\text{volume} = (\pi/6) \times \text{anteroposterior dimension} \times \text{transverse dimension} \times \text{length}$
Cervical dimensions	
Length	Distance between the ectocervical (external or distal) and endocervical (internal or proximal) margin; if this distance is measured by ultrasonography it should be done with an empty bladder and without applying pressure on the cervix
Anteroposterior dimension	Distance between the anterior and posterior aspect in the midsection of the cervical canal in the sagittal view
Transverse dimension	Distance from side to side in the transverse view in the midcervix
Cervical volume	
Three-dimensional transvaginal ultrasonography	Three-dimensional volumetric software
Formula	Cylinder: $\text{volume} = \pi \times [(\text{anteroposterior dimension} + \text{transverse dimension})/4]^2 \times \text{length}$

Table: Proposed terminology for measurement of the dimensions and volume of the cone and cervix

measured with transvaginal ultrasonography^{36,42,55} or MRI of the pelvis (appendix pp 2–3, 9).^{15,17} Cervical length with ultrasonography was defined as the distance from the external os to the internal os with an empty bladder and without applying pressure. Cervical length with MRI was also defined as the distance from the external os to the internal os. In both imaging modalities, the anteroposterior dimension was defined as the distance between the anterior margin and posterior margin of the cervix and the transverse dimension was defined as the distance between the left margin and the right margin of the cervix.

Cervical volume

In transvaginal ultrasonography, some researchers used advanced three dimensional (3D) volume calculation software to calculate cervical volume,^{36,47} whereas other researchers used formulas based on cervical dimensions to calculate cervical volume.^{42,55} In MRI, researchers used the volume formula for cylinders to calculate cervical volume (appendix pp 2–3, 9).^{15,17}

In the histopathological laboratory

The terms used in histopathological laboratories have been reported by several scientific societies and textbooks, but there are inconsistencies. The term depth was used in the 2018 guidelines published by ESGO, ESP, and the European Society for Radiotherapy and Oncology^{56,57} to describe the distance from the ectocervical edge of the cone to the endocervical edge of the cone (the greatest

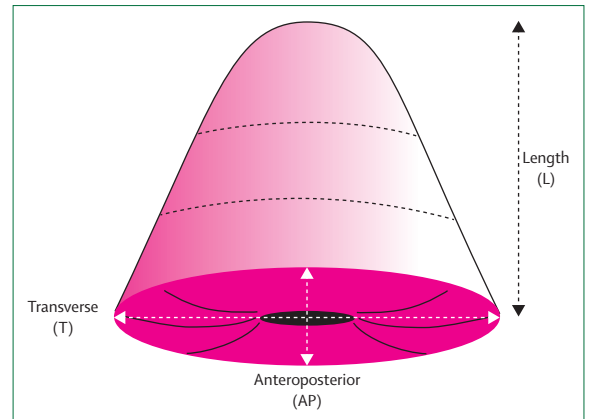


Figure 2: Proposed terminology for cone dimensions

Length is the distance of endocervical canal between the ectocervical (external or distal) and the endocervical (internal or proximal) margins. The presence or absence of preinvasive disease in both ectocervical and endocervical margins should be recorded. If margins are clear, a measurement of the distance (in mm) between the preinvasive cells and the closest resection margin can be provided, but this depends on local practice and is optional. This distance should always be recorded in the presence of invasive disease. Based on data from Public Health England⁵⁸ and the Royal College of Pathologists.⁶²

dimension perpendicular to the ectocervical surface according to the UK National Health Service histopathology recording handbook).⁵⁸ This distance was described using the term length in the 2011 European Guidelines for Quality Assurance in Cervical Histopathology⁵⁹ and by Singh and Horn,⁶⁰ and was described using the term thickness in the 2015 British Guidelines of the Royal College of Pathologists.⁶¹ The terms depth and thickness were used interchangeably in the 2018 guidelines of the International Collaboration on Cancer Reporting, which consisted of the Royal Colleges of Pathologists of Australasia and the UK, the College of American Pathologists, the Canadian Partnership Against Cancer, and ESP.²⁰

All guidelines, with the exception of the 2011 European Guidelines for Quality Assurance in Cervical Histopathology,⁵⁹ recommend the reporting of the following three cone dimensions (in mm): longitudinal or anteroposterior dimension, transverse dimension, and distance from the ectocervical edge to the endocervical edge of the cone.^{20,56,57,60,61} The European Guidelines for Quality Assurance in Cervical Histopathology are the only guidelines that report two cone dimensions (diameter and distance from the ectocervical edge to the endocervical edge of the cone; appendix p 4).⁵⁹

2022 ESGO, EFC, IFPC, and ESP terminology

The 2022 statement by ESGO, EFC, IFPC, and ESP recommends the adoption of new terminology (table, figure 2). This new terminology should be applied to all measurements of cones in both treatment centres and histopathology laboratories, as well as to measurements of the cervix by imaging. The statement was prepared following teleconferences, a compilation of comments by

each society, and an expert review. Discrepancies were resolved through discussion and a consensus was reached.

Cone dimensions and volume

The term length should be used to describe the distance of the endocervical canal between the ectocervical (external or distal) and endocervical (internal or proximal) margins. The ruler should be placed perpendicular to the external (distal) cone base. The terms depth, thickness, and height should be abandoned and replaced by the term length. The term anteroposterior dimension should be used to describe the distance between the anterior margin and posterior margin of the cone. If the cone is not oriented, the anteroposterior dimension should be randomly selected and reported. The terms longitudinal, diameter, thickness, and radius should be abandoned and replaced by the term anteroposterior dimension. A suture at the top of the cone should be used for orientation if possible, but this approach is optional.^{56,57} The term transverse dimension should be used to describe the distance between the left margin and the right margin of the cone. If the cone is not oriented, the transverse dimension should be randomly selected and reported. The terms width, thickness, and side-to-side diameter should be abandoned and be replaced by the term transverse dimension.

All three dimensions should be measured and reported (in mm) in the following order: anteroposterior dimension, transverse dimension, then length. For top hat excision (eg, additional excision of endocervical tissue after the main excision of the transformation zone), all three dimensions should be reported for both excisions. The lengths of the two excision specimens should be added together and the total length should also be recorded.⁴³ For piecemeal excisions, in which the transformation zone is removed through additional peripheral excision or excisions after the main excision, dimensions of all fragments should be recorded, but lengths should not be added together. Only the length of the main central fragment should be used to predict the risk of preterm birth in subsequent pregnancies. Castanon and colleagues³² reported that the largest length of piecemeal excisions is correlated with a similar risk of preterm birth to the risk in women who have a single-piece excision of the same length.

Measurement of the dimensions of the base of the cone (distal at ectocervix) is compulsory. Other dimensions and the dimensions of the top of the cone (proximal at endocervix) can be recorded for research purposes but are optional. Additional dimensions that can be reported include the circumference of the top and base of the cone and the lateral length (which represents the lateral dimension between the lateral ectocervical and endocervical margin). When the dimensions of both the base and top of the cone are reported, subscript B and T should be used to define the different measurements (appendix p 10).

Separate measurements before and after formalin fixation are not required but should be taken before tissue processing. Fixation in the usual concentration of 10% formalin (or 4% formaldehyde) leads to shrinkage of the sample of 0–3% (at 25°C shrinkage is 3% and at 37°C it is negligible).³⁵ On the contrary, subsequent tissue processing can lead to shrinkage of up to 20%, depending on the temperature during fixation and the quality of fixation. For example, insufficient duration of fixation might lead to greater shrinkage during tissue processing.³⁵

This guidance supports the practice that, ideally, cervical measurements should be taken by both colposcopists and pathologists. Measurements taken by colposcopists are optional but represent best practice and should be recorded in the procedure notes and on the pathology request form. Discrepancies should be assessed in future research. Measurements by colposcopists should be used in preference to pathology measurements for future risk assessment, if available. Measurements taken at time of treatment might not always be possible to obtain and are only encouraged when time restraints and clinical capacity allow. If colposcopy measurements are unable to be obtained, pathology measurements should be taken instead. Measurements taken by colposcopists are useful for several reasons. They permit direct assessment of a cone at the time of excision by the operating colposcopist, which improves measurement accuracy. The measurements can also facilitate future research or inform the need for potential further excision at time of treatment. UK clinical guidelines have recommended different lengths of excision according to the type of transformation zone (appendix p 11). Type 1 transformation zone requires an excision of 7–10 mm in length, type 2 transformation zone requires an excision of 10–15 mm in length, and type 3 transformation zone requires an excision of 15–25 mm in length.⁶³ Thickness (according to the previous IFCCPC terminology)¹⁹ of less than 2.9 mm is suggested to increase the risk of involved stromal margin.⁶⁴ Furthermore, the knowledge and documentation of cone dimensions in the clinic by the colposcopist can inform counselling and antenatal management in subsequent pregnancies.

Measurement of cone volume is optional and currently considered experimental. The volume value should be recorded, if available, for research purposes and not for clinical use. Further research is required to explore how cone volume correlates to clinical outcomes and how it compares with cone length as a predictor of all outcomes. The fluid displacement technique should be used for measurement. If this technique is not feasible, cone volume should be calculated using the volume formula for a semi-ellipsoid (table). Although volume formulas for several shapes have previously been used to measure cone volume, including the cone, the parallelepiped, and the frustum (truncated cone), the semi-ellipsoid is a more accurate depiction of the true curvature of the proximal side of the cone.⁶⁵ Furthermore, the

semi-ellipsoid calculation only requires three dimensions that are measured routinely (anteroposterior dimension, transverse dimension, and length). Different formulas can be used based on clinical judgement if different cone shapes are present (appendix pp 7–8).

Cervical dimensions and volume

New proposed terminology (anteroposterior dimension, transverse dimension, and length) should be used in ultrasonography or MRI for the description of cervical dimensions. In ultrasonography, 3D volumetry should be used to calculate cervical volume. If 3D volumetry is not available, cervical volume can be calculated from the cervical dimensions using the cylinder formula (table). Measurements of cervical dimensions and volume of the whole cervix are optional and currently considered experimental. These measurements should be recorded, if available, for research purposes and not for clinical use. Further research is required to explore how the proportion of removed cervical length or volume correlates to clinical outcomes.

Discussion and clinical use

The 2022 statement by ESGO, EFC, IFCPC, and ESP recommends the introduction of and universal use of a single set of terminology in both the clinic and the histopathology laboratory that can facilitate more accurate and effective communication of results, clinical decision making, and patient counselling. This terminology will improve recording of results, future research, and meta-analyses.

The rigorous reporting of dimensions should be available for effective patient counselling at colposcopy clinics and antenatal clinics.³⁰ The majority of women undergoing treatment for SIL or CIN are younger than 40 years,⁴ so the introduction of standardised terminology could assist in making antenatal management and interventions more effective when trying to prevent reproductive complications, stratified to individual risk. The knowledge that SIL or CIN treatment increases the

risk of preterm birth has led to major changes in clinical practice, not only in colposcopy but also in antenatal care. Many obstetrical units have introduced cervical length measurement for women with history of conisation and, if necessary, preventive treatments such as cervical cerclage, progesterone, and antenatal corticosteroid therapy are given.⁶⁶ However, practices across obstetrical units vary and are resource-dependent, unit-dependent, and clinician-dependent. In some clinical settings, cervical length measurement for women with history of conisation has become the standard of care without strong evidence of its benefit.⁶⁶ In other clinical settings, only women with either cone length more than 10 mm or repeat conisations are offered antenatal interventions.

The accurate prospective recording of cone and cervix dimensions will permit further research to stratify women by risk of poor reproductive outcomes antenatally and offer risk-limiting interventions to those most at risk, particularly in limited-resource settings. Furthermore, measurement of dimensions of either cones or cervixes at treatment centres and clinics could further improve treatment quality and margin clearance.⁶³ Existing colposcopy databases should be adapted to routinely document the proposed dimensions and volumes and collect prospective long-term data on both oncological outcomes and reproductive outcomes. Increasing cone length at local treatment has been previously associated with reduced risk of lesion recurrence¹⁸ and higher rates of preterm birth.¹³ Data from prospective databases could provide further evidence on the optimal treatment methods and length of excision for different transformation zone types. A network meta-analysis exploring these comparisons and the existing evidence base was published in 2022.³⁴

Conclusion

This Series paper introduces the terminology for cone and cervical dimensions proposed by ESGO, EFC, IFCPC, and ESP in 2022. It is recommended that this new terminology replace all existing terms in clinical and research settings. Professional bodies worldwide should disseminate this terminology and recommend that treatment centres, radiologists, and histopathologists should measure and report the three dimensions using standardised methods (anteroposterior dimension, transverse dimension, and length). Consistent use of the new terminology across settings would allow effective counselling in colposcopy clinics and accurate risk stratification in antenatal clinics, while making interventions more accurate and effective. Universally consistent reporting will facilitate improved communications between clinicians and pathologists, promote assessment of quality of practice and future research, and improve the quality of future meta-analyses.

Contributors

The manuscript was conceived by MK and EP. MK, MA, MG, and EP designed and led the work presented. The literature search was conducted

Search strategy and selection criteria

We searched PubMed from inception until Jan 10, 2019, to identify articles on terminology and measurement of the dimensions or volume of cervix or excised cone (appendix p 1). There were no language restrictions. Additionally, we manually searched for guidelines from gynaecological and pathology societies, and we searched the reference lists of our most recent meta-analyses. Search results were discussed among members of the European Society of Gynaecologic Oncology (ESGO), the European Federation for Colposcopy (EFC), the International Federation of Cervical Pathology and Colposcopy (IFCPC), and the European Society of Pathology (ESP) before reaching a consensus. We included 66 references in this Series paper.

by MK and AA. Retrieved studies, personal experiences, and opinions were discussed among all authors. The manuscript was drafted by MK, AA, and EP, and was critically revised by all authors. All authors agreed with the results and conclusions presented in this Series paper.

Declaration of interests

We declare no competing interests.

Acknowledgments

This work has been funded by ESGO and EFC (P78368). MK and AA were funded by the National Institute for Health and Care Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0816-20004). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. MA was also supported by the Horizon 2020 Framework Programme for Research and Innovation of the European Commission through the Risk-based Screening for Cervical Cancer Network (847845), and by ESGO.

References

- 1 International Agency for Research on Cancer. Cervix cancer screening: IARC handbooks of cancer prevention. Lyon: IARC Press, 2005: 1–302.
- 2 Kyrgiou M, Arbyn M, Bergeron C, et al. Cervical screening: ESGO-EFC position paper of the European Society of Gynaecologic Oncology (ESGO) and the European Federation of Colposcopy (EFC). *Br J Cancer* 2020; **123**: 510–17.
- 3 International Agency for Research on Cancer. WHO classification of tumours: female genital tumours. 5th edn. Lyon: IARC Press, 2020.
- 4 Public Health England. Cervical screening programme, England-2020–21. 2021. <https://digital.nhs.uk/data-and-information/publications/statistical/cervical-screening-annual/england--2020-2021> (accessed June 12, 2022).
- 5 Joura EA, Kyrgiou M, Bosch FX, et al. Human papillomavirus vaccination: the ESGO-EFC position paper of the European Society of Gynaecologic Oncology and the European Federation for Colposcopy. *Eur J Cancer* 2019; **116**: 21–26.
- 6 Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 2020; **24**: 102–31.
- 7 Jo's Cervical Cancer Trust. LLETZ. <https://www.jostrust.org.uk/information/cervical-cancer/treatments/surgery/lletz> (accessed June 12, 2022).
- 8 Jo's Cervical Cancer Trust. Cone biopsy. <https://www.jostrust.org.uk/information/cervical-cancer/treatments/surgery/cone-biopsy> (accessed June 12, 2022).
- 9 Prendiville W, Sankaranarayanan R. Treatment of cervical intraepithelial neoplasia (CIN). Colposcopy and treatment of cervical precancer. Lyon: IARC Press, 2017: 85–89.
- 10 Kyrgiou M, Koliopoulos G, Martin-Hirsch P, Arbyn M, Prendiville W, Paraskevaidis E. Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis. *Lancet* 2006; **367**: 489–98.
- 11 Kyrgiou M, Mitra A, Arbyn M, et al. Fertility and early pregnancy outcomes after treatment for cervical intraepithelial neoplasia: systematic review and meta-analysis. *BMJ* 2014; **349**: g6192.
- 12 Kyrgiou M, Mitra A, Arbyn M, et al. Fertility and early pregnancy outcomes after conservative treatment for cervical intraepithelial neoplasia. *Cochrane Database Syst Rev* 2015; **9**: CD008478.
- 13 Kyrgiou M, Athanasiou A, Paraskevaidi M, et al. Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: systematic review and meta-analysis. *BMJ* 2016; **354**: i3633.
- 14 Kyrgiou M, Athanasiou A, Kalliala IEJ, et al. Obstetric outcomes after conservative treatment for cervical intraepithelial lesions and early invasive disease. *Cochrane Database Syst Rev* 2017; **11**: CD012847.
- 15 Founta C, Arbyn M, Valasoulis G, et al. Proportion of excision and cervical healing after large loop excision of the transformation zone for cervical intraepithelial neoplasia. *BJOG* 2010; **117**: 1468–74.
- 16 Khalid S, Dimitriou E, Conroy R, et al. The thickness and volume of LLETZ specimens can predict the relative risk of pregnancy-related morbidity. *BJOG* 2012; **119**: 685–91.
- 17 Kyrgiou M, Valasoulis G, Stasinou SM, et al. Proportion of cervical excision for cervical intraepithelial neoplasia as a predictor of pregnancy outcomes. *Int J Gynaecol Obstet* 2015; **128**: 141–47.
- 18 Ang C, Mukhopadhyay A, Burnley C, et al. Histological recurrence and depth of loop treatment of the cervix in women of reproductive age: incomplete excision versus adverse pregnancy outcome. *BJOG* 2011; **118**: 685–92.
- 19 Bornstein J, Bentley J, Bösze P, et al. 2011 colposcopic terminology of the International Federation for Cervical Pathology and Colposcopy. *Obstet Gynecol* 2012; **120**: 166–72.
- 20 McCluggage WG, Judge MJ, Alvarado-Cabrero I, et al. Data set for the reporting of carcinomas of the cervix: recommendations from the International Collaboration on Cancer Reporting (ICCR). *Int J Gynecol Pathol* 2018; **37**: 205–28.
- 21 Arbyn M, Redman CWE, Verdoodt F, et al. Incomplete excision of cervical precancer as a predictor of treatment failure: a systematic review and meta-analysis. *Lancet Oncol* 2017; **18**: 1665–79.
- 22 Martin-Hirsch PPL, Paraskevaidis E, Bryant A, Dickinson HO. Surgery for cervical intraepithelial neoplasia. *Cochrane Database Syst Rev* 2013; **12**: CD001318.
- 23 Kyrgiou M, Bowden SJ, Athanasiou A, et al. Morbidity after local excision of the transformation zone for cervical intra-epithelial neoplasia and early cervical cancer. *Best Pract Res Clin Obstet Gynaecol* 2021; **75**: 10–22.
- 24 Strander B, Hällgren J, Sparén P. Effect of ageing on cervical or vaginal cancer in Swedish women previously treated for cervical intraepithelial neoplasia grade 3: population based cohort study of long term incidence and mortality. *BMJ* 2014; **348**: f7361.
- 25 Athanasiou A, Veroniki AA, Efthimiou O, et al. Comparative efficacy and complication rates after local treatment for cervical intraepithelial neoplasia and stage 1a1 cervical cancer: protocol for a systematic review and network meta-analysis from the CIRCLE Group. *BMJ Open* 2019; **9**: e028008.
- 26 Bae HS, Chung YW, Kim T, Lee KW, Song JY. The appropriate cone depth to avoid endocervical margin involvement is dependent on age and disease severity. *Acta Obstet Gynecol Scand* 2013; **92**: 185–92.
- 27 Mitra A, Kindinger L, Kalliala I, et al. Obstetric complications after treatment of cervical intraepithelial neoplasia. *Br J Hosp Med (Lond)* 2016; **77**: C124–27.
- 28 Wuntakal R, Castanon A, Landy R, Sasieni P. How many preterm births in England are due to excision of the cervical transformation zone? Nested case control study. *BMC Pregnancy Childbirth* 2015; **15**: 232.
- 29 Arbyn M, Kyrgiou M, Simoens C, et al. Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis. *BMJ* 2008; **337**: a1284.
- 30 Kyrgiou M, Martin-Hirsch PPL, Paraskevaidis E, Bennett PR. Reproductive outcomes after local treatment for preinvasive cervical disease. London: Royal College of Obstetricians and Gynaecologists, 2016. <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/sip21/> (accessed June 12, 2020).
- 31 Noehr B, Jensen A, Frederiksen K, Tabor A, Kjaer SK. Depth of cervical cone removed by loop electrosurgical excision procedure and subsequent risk of spontaneous preterm delivery. *Obstet Gynecol* 2009; **114**: 1232–38.
- 32 Castanon A, Landy R, Brocklehurst P, et al. Risk of preterm delivery with increasing depth of excision for cervical intraepithelial neoplasia in England: nested case-control study. *BMJ* 2014; **349**: g6223.
- 33 Athanasiou A, Veroniki AA, Efthimiou O, et al. Comparative fertility and pregnancy outcomes after local treatment for cervical intraepithelial neoplasia and stage 1a1 cervical cancer: protocol for a systematic review and network meta-analysis from the CIRCLE group. *BMJ Open* 2019; **9**: e028009.
- 34 Athanasiou A, Veroniki AA, Efthimiou O, et al. Comparative effectiveness and reproductive morbidity of local treatments for cervical intraepithelial neoplasia and stage 1a1 cervical cancer: a systematic review and network meta-analysis. *Lancet Oncol* (in press).
- 35 Fox CH, Johnson FB, Whiting J, Roller PP. Formaldehyde fixation. *J Histochem Cytochem* 1985; **33**: 845–53.
- 36 Papoutsis D, Rodolakis A, Mesogitis S, Sotiropoulou M, Antsaklis A. Regeneration of uterine cervix at 6 months after large loop excision of the transformation zone for cervical intraepithelial neoplasia. *BJOG* 2012; **119**: 678–84.

- 37 Rubio CA, Thomassen P, Kock Y. Influence of the size of cone specimens on postoperative hemorrhage. *Am J Obstet Gynecol* 1975; **122**: 939–44.
- 38 Paraskevaïdis E, Bilirakis E, Koliopoulos G, et al. Cervical regeneration after diathermy excision of cervical intraepithelial neoplasia as assessed by transvaginal sonography. *Eur J Obstet Gynecol Reprod Biol* 2002; **102**: 88–91.
- 39 Papoutsis D, Rodolakis A, Mesogitis S, Sotiropoulou M, Antsaklis A. Appropriate cone dimensions to achieve negative excision margins after large loop excision of transformation zone in the uterine cervix for cervical intraepithelial neoplasia. *Gynecol Obstet Invest* 2013; **75**: 163–68.
- 40 Halliwell DE, Kyrgiou M, Mitra A, et al. Tracking the impact of excisional cervical treatment on the cervix using biospectroscopy. *Sci Rep* 2016; **6**: 38921.
- 41 Preaubert L, Gondry J, Mancini J, et al. Benefits of direct colposcopic vision for optimal LLETZ procedure: a prospective multicenter study. *J Low Genit Tract Dis* 2016; **20**: 15–21.
- 42 Ciavattini A, Delli Carpini G, Moriconi L, et al. Effect of age and cone dimensions on cervical regeneration: an Italian multicentric prospective observational study. *BMJ Open* 2018; **8**: e020675.
- 43 Ortoft G, Henriksen T, Hansen E, Petersen L. After conization of the cervix, the perinatal mortality as a result of preterm delivery increases in subsequent pregnancy. *BJOG* 2010; **117**: 258–67.
- 44 Phadnis SV, Atilade A, Young MP, Evans H, Walker PG. The volume perspective: a comparison of two excisional treatments for cervical intraepithelial neoplasia (laser versus LLETZ). *BJOG* 2010; **117**: 615–19.
- 45 Grisot C, Mancini J, Giusiano S, et al. How to optimize excisional procedures for the treatment of CIN? The role of colposcopy. *Arch Gynecol Obstet* 2012; **285**: 1383–90.
- 46 Carcopino X, Mancini J, Charpin C, et al. Direct colposcopic vision used with the LLETZ procedure for optimal treatment of CIN: results of joint cohort studies. *Arch Gynecol Obstet* 2013; **288**: 1087–94.
- 47 Carcopino X, Maycock JA, Mancini J, et al. Image assessment of cervical dimensions after LLETZ: a prospective observational study. *BJOG* 2013; **120**: 472–78.
- 48 Grimm C, Brammen L, Sliutz G, et al. Impact of conization type on the resected cone volume: results of a retrospective multi-center study. *Arch Gynecol Obstet* 2013; **288**: 1081–86.
- 49 Kitson SJ, Greig E, Michael E, Smith M. Predictive value of volume of cervical tissue removed during LLETZ on subsequent preterm delivery: a cohort study. *Eur J Obstet Gynecol Reprod Biol* 2014; **180**: 51–55.
- 50 Ciavattini A, Clemente N, Delli Carpini G, et al. Loop electrosurgical excision procedure and risk of miscarriage. *Fertil Steril* 2015; **103**: 1043–48.
- 51 Martyn FM, McAuliffe FM, Beggan C, Downey P, Flannelly G, Wingfield MB. Excisional treatments of the cervix and effect on subsequent fertility: a retrospective cohort study. *Eur J Obstet Gynecol Reprod Biol* 2015; **185**: 114–20.
- 52 Liverani CA, Di Giuseppe J, Clemente N, et al. Length but not transverse diameter of the excision specimen for high-grade cervical intraepithelial neoplasia (CIN 2–3) is a predictor of pregnancy outcome. *Eur J Cancer Prev* 2016; **25**: 416–22.
- 53 Öz M, Çetinkaya N, Korkmaz E, Seçkin KD, Meydanlı MM, Güngör T. Optimal cone size to predict positive surgical margins after cold knife conization (CKC) and the risk factors for residual disease. *J Turk Ger Gynecol Assoc* 2016; **17**: 159–62.
- 54 Leiman G, Harrison NA, Rubin A. Pregnancy following conization of the cervix: complications related to cone size. *Am J Obstet Gynecol* 1980; **136**: 14–18.
- 55 Song T, Seong SJ, Kim BG. Regeneration process after cervical conization for cervical intraepithelial neoplasia. *Obstet Gynecol* 2016; **128**: 1258–64.
- 56 Cibula D, Pötter R, Planchamp F, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. *Virchows Arch* 2018; **472**: 919–36.
- 57 Raspollini MR, Lax SF, McCluggage WG. The central role of the pathologist in the management of patients with cervical cancer: ESGO/ESTRO/ESP guidelines. *Virchows Arch* 2018; **473**: 45–54.
- 58 Public Health England. Cervical screening programme: histopathology reporting handbook. 2021. <https://www.gov.uk/government/publications/cervical-screening-histopathology-reporting-handbook/cervical-screening-programme-histopathology-reporting-guidance> (accessed June 12, 2022).
- 59 Bulten J, Horvat R, Jordan J, Herbert A, Wiener H, Arbyn M. European guidelines for quality assurance in cervical histopathology. *Acta Oncol* 2011; **50**: 611–20.
- 60 Singh N, Horn LC. Appendix 1: surgical cut up of cervical specimens. 2017. <https://link.springer.com/content/pdf/bbm%3A978-3-319-51257-0%2F1.pdf> (accessed June 12, 2022).
- 61 RCPATH. Tissue pathways for gynaecological pathology. 2015. <https://www.rcpath.org/uploads/assets/94763195-0982-40ed-bbc79ca92370e9ac/Tissue-pathways-for-gynaecological-pathology-January-2015.pdf> (accessed June 12, 2022).
- 62 RCPATH. Appendix C: Reporting proforma for cervical cancer in excisional cervical biopsies. 2021. <https://www.rcpath.org/resourceLibrary/appendix-c-reporting-proforma-for-cervical-cancer-in-excisional-cervical-biopsies.html> (accessed June 12, 2022).
- 63 Public Health England. NHS cervical screening programme: colposcopy and programme management. 2016. <https://www.gov.uk/government/publications/cervical-screening-programme-and-colposcopy-management> (accessed June 12, 2022).
- 64 Anderson MC, Hartley RB. Cervical crypt involvement by intraepithelial neoplasia. *Obstet Gynecol* 1980; **55**: 546–50.
- 65 Carcopino X, Mancini J, Prendiville W, et al. The accuracy of large loop excision of the transformation zone specimen dimensions in determining volume: a multicentric prospective observational study. *J Low Genit Tract Dis* 2017; **21**: 120–24.
- 66 Kindinger LM, Kyrgiou M, MacIntyre DA, et al. Preterm birth prevention post-conization: a model of cervical length screening with targeted cerclage. *PLoS One* 2016; **11**: e0163793.