Clinical Oncology

Gynaecological cancer: RCR consensus statements

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The Royal College of Radiologists

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RCR gynaecological cancer consensus statements

These statements should be read in conjunction with the accompanying explanatory notes.

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1.2 Review multiple image modalities to aid target delineation.
1.3 Consider multiple planning scans to model target motion.

Radiotherapy technique

1.4 Offer treatment with intensity modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) for all radical cases and appropriate palliative treatments, with simultaneous integrated boost (SIB) for clinically involved nodes.

Treatment delivery training and quality assurance (QA)

1.5 Offer daily 3D volumetric imaging for mobile targets using the largest collimator. Use extended 3D imaging tools for extended field treatments.
1.6 Offer a soft-tissue adaptive approach when using daily volumetric imaging. Set defined action levels for online correction, intervention and use of adaptive plans.
1.7 Ensure access to a treatment centre training programme is in place for image-guided (IG) and adaptive radiotherapy (ART) for clinicians and advanced radiographer practice.
1.8 Arrange regular multiprofessional meetings to review individual patient factors such as pre-treatment set-up and planning, peer review of contouring, ART, verification imaging and on-treatment care. Audit of local practice is encouraged.

ART aspirations

1.9 Consider an interim goal of daily proactive ART, for example a library ‘plan of the day’ approach.
1.10 Consider a future goal of daily online replanning with the availability of specific hardware and planning software.

Topic 2: Brachytherapy

Assessing competencies and minimum numbers

2.1 Recommend a minimum of 10 insertions (rather than number of patients) per clinician per year incorporating peer review (live or retrospective) in the contouring pathway.
2.2 Offer all specialist registrars adequate experience in brachytherapy during their training. All specialist registrars should observe brachytherapy cases; more in-depth expertise will require elective placement or Fellowship training.

Use of interstitial brachytherapy

2.3 Offer interstitial brachytherapy where clinically appropriate. A referral pathway should be in place to centres of expertise if not available locally.
2.4 Consider magnetic resonance imaging (MRI) within the week prior to first brachytherapy insertion to aid applicator selection including placement of interstitial needles.
2.5 Offer MRI-based planning for interstitial brachytherapy.

Recommendations regarding scheduling

2.6 Consider treating no more than 2 brachytherapy fractions per insertion.

Topic 3: Imaging and follow-up including late effects

Imaging following definitive radiotherapy

3.1 Offer post-treatment imaging to assess radiological response and facilitate detection of salvageable recurrence if appropriate.
3.2 Offer MRI at 3 months post treatment and consider positron emission tomography-computed tomography (PET-CT). Consider interval MRI imaging for cancer that is regressing but has not resolved at the 3-month scan.
3.3 Offer PET-CT if residual or progressive disease on MRI and a radical surgical option is available and appropriate.
3.4 For early detection of locoregional recurrence consider MR imaging of the pelvis, plus retroperitoneum if appropriate, at 1 year.
3.5 For early detection of oligometastatic disease, offer CT imaging at 1 year and consider additional imaging beyond 1 year.

Salvage surgery

Also refer to the reirradiation section (topic 4)

3.6 Consider salvage surgery by a specialist surgical team for histologically proven persistent or recurrent disease within the treatment field after definitive radiotherapy in order to achieve locoregional control, using the least morbid approach that will permit an R0 resection margin.

Late effects

3.7 Offer pre-radiotherapy intervention to optimise health and minimise late effects, including smoking cessation and education on diet, hydration, physical activity, lifestyle factors, self-management tools and psychosocial support.
3.8 Offer access to a comprehensive late effects service encompassing chronic pelvic pain, lymphoedema, menopause, mental health issues, sexual problems, and bone, dermatological, gastrointestinal, neurological or urological toxicity.

Follow-up

3.9 Consider personalised stratified follow-up based on risk of recurrence and toxicity. In selected patients this may include patient-initiated follow-up (PIFU) via a designated member of the multidisciplinary team (MDT) (eg specialist nurse or radiographer).
3.10 Ensure there is a well-defined pathway for patient access to rapid assessment in the event of suspected recurrence and/or development of late effects.

Topic 4: Reirradiation of gynaecological cancers

These statements should be used in conjunction with The Royal College of Radiologists principles of reirradiation guidance (see reirradiation section topic 4).

4.1 Offer multimodality imaging (using diffusion-weighted MRI, PET-CT and radiotherapy CT planning scan) to assess the extent of disease accurately.
4.2 Consider reirradiation for isolated lymph node (LN) or pelvic soft tissue recurrence. Examples of suitable targets for a repeat course of radiation include:
   a. Oligometastatic pelvic LN relapse
   b. Oligometastatic soft tissue recurrences (eg vaginal vault, lower vagina, peritoneum)
   c. Unexpected positive margins following salvage surgery
   d. Palliation of recurrent pelvic disease.

Quality assurance for reirradiation

4.3 Review all reirradiation cases in MDT and peer review meetings. If not offered locally, cases should be discussed in centres that offer more advanced techniques such as stereotactic body radiotherapy (SBRT) and interstitial brachytherapy.

Reirradiation technique

4.4 Offer the most appropriate technique to adequately encompass disease and accommodate organ-at-risk (OAR) dose.
4.5 Offer stereotactic radiotherapy for metachronous oligometastatic disease (<5–6 cm max. dimension, OAR constraints achievable).
4.6 Consider interstitial brachytherapy for central pelvic or vaginal relapse.
4.7 Consider VMAT or IMRT for palliative reirradiation cases.

Data collection for reirradiation

4.8 Register all cases in any available national reirradiation audit and future national databases to inform further guidelines and the development of specific protocols or dosimetric constraints.

Topic 5: Molecular testing and sentinel lymph node assessment in endometrial cancer

Molecular testing

5.1 Ensure access to immunohistochemistry or molecular testing for mismatch repair (MMR) (followed by hypermethylation testing where necessary) oestrogen receptors (ER) and p53 and next-generation DNA sequencing for POLE in all centres.

5.2 All immunohistochemistry and/or molecular testing results should be available less than 6 weeks from diagnostic biopsy to ensure timely delivery of adjuvant therapy and enable trial recruitment.

5.3 Offer adjuvant treatment based on a combination of pathology parameters including stage, histopathology and molecular classification.

Sentinel nodes

5.4 Offer sentinel nodal biopsy with ultra-staging with the purpose of guiding adjuvant therapy and sparing patients the morbidity of pelvic nodal dissection and combined modality treatment.

5.5 Collection of prospective data on outcomes and participation in clinical trials are encouraged.

Introduction

The Royal College of Radiologists' consensus statements are produced to guide and support clinicians in controversial areas of practice that lack strong evidence. They aim to reduce variation in UK cancer care and to support development towards best practice across the UK. These gynaecological cancer consensus statements follow from excellent work done by the RCR in other cancer sites.[1–6] They follow a robust process outlined below.

Previous RCR audits and surveys in gynaecological cancers have shown that variation in practice across the country has decreased following introduction of national recommendations, demonstrating the value of support from the RCR when striving to achieve consistent and optimal care for patients.[7–9] When developing these consensus statements, the committee felt it was not only important to focus on the cancer treatment but also to recognise that oncology treatment can come with associated toxicity. Thus, it is important not only to treat the cancer but to ensure that patients are able to live well after cancer treatment, with access to a full range of services that minimise the effects of cancer and its treatment on them and their families. We also wanted to focus on technological development, recognising that limited resources may slow the introduction of some of the more advanced technologies, but we should strive towards interim and future solutions that can be used to improve both quality of life and cure.

The consensus group aim is for the statements to be used by MDTs as a stimulus to drive local improvements and support local service development.

We are extremely grateful to Sarah Griffin for her support in producing this work. We acknowledge the time, effort and commitment of the committee, the stakeholder associations and the participants in the consensus meeting.

Alexandra Stewart, chair of the Gynaecological Consensus Steering Group

Nicky Thorp, Medical Director for Professional Practice, Clinical Oncology Faculty, RCR

What are consensus statements?

Consensus statements are developed by a group of experts on a topic for which 'consensus is sought using an explicit methodology to identify areas of agreement and disagreement'.[10] The consensus statements reflect the group's collective analysis and evaluation of the best available evidence as well as their expert opinion on a topic.

Clinical consensus statements are separate from clinical practice guidelines. While both provide recommendations on clinical practice, there are subtle but important differences. Clinical guidelines are usually based on a formal systematic review of high-level evidence, while consensus statements are most appropriate on topics where evidence is limited or lacking and therefore where a consensus approach offers the best way to address variability in clinical practice and improve patient outcomes.[11]

The RCR consensus methodology

The RCR consensus statements[1,2,4–6] are produced to guide and support clinicians in controversial areas of practice that lack strong evidence. They aim to reduce unacceptable variation in UK radiotherapy and cancer care.

Gynaecological cancer experts were recruited to a steering group to develop a series of consensus statements around gynaecological cancer practice for the RCR. This multidisciplinary group included clinical oncologists, therapeutic radiographers, medical physicists, a gynaecological oncologist, a radiologist and a senior programme manager from Living With & Beyond Cancer at NHS England, and a Pelvic Radiation Disease Association trustee, ensuring the representation of patients was included.

The group was asked to focus on topics where there was current variation in the UK and to avoid duplicating other guidelines unless there were good reasons for reiterating them. The topics that were chosen reflect current areas of challenge within gynaecological cancer in the UK with a significant national variation in available technology, technical expertise and post-treatment care. The group focused on areas where decreasing variation or introducing different techniques or approaches are likely to lead to the greatest benefit to patients, either in survival and cure or in quality of life after treatment.

Five broad topic areas were selected. Following an appraisal of the available research literature, statements were drafted and refined over a six-month period.

Gynaecological cancer radiotherapy leads from all UK cancer centres were invited to share the first draft statements with their MDTs and to provide feedback. The draft statements were also shared with relevant stakeholders including British Gynaecological Cancer Society, Society and College of Radiographers, Institute of Physics and Engineering in Medicine, Association of Cancer Physicians, Royal College of Anaesthetists, Royal College of Pathologists, British Society of Urogenital Radiology, Pelvic Radiation Disease Association, The Eve Appeal, Jo's Cervical Cancer Trust and Go Girls.

All feedback received was reviewed in detail by the steering group and the statements and accompanying notes revised for consideration at a consensus meeting.

In advance of the consensus meeting, these revised draft statements were circulated to all gynaecological cancer radiotherapy leads.

On 13 September 2023 gynaecological cancer radiotherapy leads from each centre were invited to attend a virtual consensus meeting to discuss and vote on the draft statements. Representatives were present from 44 centres, along with members of the steering group and a gynaecological cancer patient representative.

Following initial discussions in small breakout groups a whole-group discussion was facilitated by the steering group. Several statements were refined based on the meeting discussions. Representatives were then asked to vote on each statement on behalf of their centre, with one vote per centre.

The following voting categories were agreed to indicate strength of voting. Consensus in the responses was defined as agreement among at least 70% of participants.

Unanimous support	100%
Very strongly supported	90–99%
Strongly supported	70–89%
Majority support	60–69%
Equipoise	50–59%
Rejected	< 50%

Members of the steering group took notes of the discussion.

The final statements were then approved by the RCR's Clinical Oncology Professional Support and Standards Board for publication.

Wording the consensus statements

Most of the RCR statements have been worded to make them concise, unambiguous and easy to translate into practice.

The wording of the RCR statements is based on the National Institute for Health and Care Excellence (NICE) technical manual.[12]

Most of the statements start with a verb describing what the reader should do. The verb chosen reflects the strength of the recommendation.

- Statements of what should (or should not) be offered use directive language such as 'offer' (or 'do not offer'), 'delineate', 'omit', 'treat' and so on.
- If there is a closer balance between benefits and harms the statement starts with 'consider'. These are recommendations for activities or interventions that *could* be used but where discussion with clinical teams and the patient, carefully considering the alternatives, is advised.

Definitions

- **Definitive radiotherapy**, with chemotherapy as indicated for medically fit patients, is recommended to treat patients with potentially curable tumours that are unresectable or not fit for curative surgical resection.
- **Radical radiotherapy** refers to treatment courses which use radiation doses that take surrounding tissues up to, or close to, normal tissue tolerance. These are usually curative in nature and include both definitive and adjuvant radiotherapy.
- **Palliative radiotherapy** refers to treatment courses that use lower radiation doses aiming for symptom control and/or disease shrinkage and is generally recommended for less fit patients or those with metastatic disease.

01 Image-guided and adaptive radiotherapy (IG-ART) for mobile gynaecological targets

Topic 1 statements

Statement		Voting outcome
Treatment preparation		
1.1	Offer a drinking protocol and consider bowel preparation for radical gynaecological radiotherapy treatments that are subject to bladder and rectal dependent motion.	Unanimous support
1.2	Review multiple image modalities to aid target delineation.	Unanimous support
1.3	Consider multiple planning scans to model target motion.	Very strongly supported
Radiotherapy technique		
1.4	Offer treatment with intensity modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) for all radical cases and appropriate palliative treatments, with simultaneous integrated boost (SIB) for clinically involved nodes.	Unanimous support
Treatment delivery training and quality assurance (QA)		
1.5	Offer daily 3D volumetric imaging for mobile targets using the largest collimator. Use extended 3D imaging tools for extended field treatments.	Unanimous support
1.6	Offer a soft tissue adaptive approach when using daily volumetric imaging. Set defined action levels for online correction, intervention and use of adaptive plans.	Strongly supported
1.7	Ensure access to a treatment centre training programme is in place for image-guided (IG) and adaptive radiotherapy (ART) for clinicians and advanced radiographer practice.	Very strongly supported
1.8	Arrange regular multiprofessional meetings to review individual patient factors such as pre-treatment set-up and planning, peer review of contouring, ART, verification imaging and on-treatment care. Audit of local practice is encouraged.	Very strongly supported
ART aspirations		
1.9	Consider an *interim goal* of daily proactive ART, for example a library 'plan of the day' approach.	Very strongly supported
1.10	Consider a *future goal* of daily online replanning with the availability of specific hardware and planning software.	Strongly supported

01
Topic 1: IG-ART

Topic 1 explanatory notes

The uterus-cervix is the mobile gynaecological target for which adaptive radiotherapy strategies are most commonly used.[13] However, the topic 1 IG-ART statements may also apply to the vaginal vault following hysterectomy or vaginal cancers. The principles may also apply for SIB, especially in tumours that shrink rapidly in response to radiotherapy treatment.

Standardised daily pre-treatment preparation minimises target motion and protects normal tissues; for example, emptying the bladder then drinking approximately 500–600 ml of water and waiting 30–60 minutes, or use of regular laxatives or enemas to minimise the effects of faecal loading. Local centres should use their preferred schedules for drinking and laxative use in a prospective or reactive way. Further examples of treatment preparation are given in the protocols for the EMBRACE-II[14] and PORTEC-3[15] trials and the ESGO-ESTRO-ESP guidance for endometrial cancer.[16] These recommendations vary in the level of detail due to marked inter-patient and intrapatient variability.

The generation of an integrated target volume (ITV) can be informed by the variable OAR positions from images taken at the time of planning and at diagnosis. The use of multiple image modalities may include using empty and full bladder planning CT scans and/or reviewing diagnostic MRI and PET-CT scan images to assess the range of organ motion. More complex techniques such as MR fusion with the radiotherapy planning CT scan or CT scanning with multiple levels of bladder filling may not be time efficient in a busy cancer centre. However, the use of the available diagnostic images (MR and PET-CT) and the gradual introduction of more than one radiotherapy planning scan to assess the effect of bladder movement on the target will aid the ability of the centre to further develop adaptive radiotherapy techniques.

The EMBRACE-II protocol is a useful reference for the use of SIB, giving further information on doses and organ tolerances.[14]

Daily 3D volumetric imaging for all treatments, other than simple palliative plans, can aid accuracy of radiotherapy delivery and is recommended.

When using daily soft tissue matching, registration of 3D imaging is to bone anatomy at set-up, then assessment of appropriate actions should be undertaken. These include couch moves, getting the patient off the couch for alteration of bladder filling or to attain a change in rectal gas, selection of a library plan or assessment and editing of online adapted plans. The aim is to keep the times a patient is taken off the couch to a minimum. It must always be ensured that the elective nodal field and SIB target coverage are not compromised due to patient twist or other factors.

Healthcare professional training is required for progressive competencies for soft tissue matching, choosing the appropriate action for intervention and plan selection from a library of plans[17,18] or online adapted plans.[19]

Multiprofessional meetings and peer review are encouraged to discuss local implementation of IG-ART. The involvement of a multiprofessional team, which may include radiographers, physicists, clinicians, specialist advanced clinical practitioners (ACPs) or radiologists, will help with assessing, planning and reviewing radiotherapy treatments and will also aid the progress of technique development within each department. How this is organised will depend on local set-up, capacity and the ability to coordinate workflow for a range of professionals. However, it is agreed that this is beneficial to service development and patient care.

01

Topic 1: IG-ART

ART implementation is complex and time-consuming for all involved in treatment planning and delivery, but it carries significant benefit since the large volume expansions required for non-adaptive gynaecological treatments due to internal organ movement and changes in the target inevitably increase the dose to uninvolved organs. Offline and online ART techniques are developing and are being implemented in radiotherapy departments. This is a very important area of development that can be introduced in increments within radiotherapy departments.

02 Brachytherapy

Topic 2 statements

Statement		Voting outcome
Assessing competencies and minimum numbers		
2.1	Recommend a minimum of 10 insertions (rather than number of patients) per clinician per year incorporating peer review (live or retrospective) in the contouring pathway.	Very strongly supported
2.2	Offer all specialist registrars adequate experience in brachytherapy during their training. All specialist registrars should observe brachytherapy cases; more in-depth expertise will require elective placement or Fellowship training.	Unanimous support
Use of interstitial brachytherapy		
2.3	Offer interstitial brachytherapy where clinically appropriate. A referral pathway should be in place to centres of expertise if not available locally.	Unanimous support
2.4	Consider magnetic resonance imaging (MRI) within the week prior to first brachytherapy insertion to aid applicator selection including placement of interstitial needles.	Very strongly supported
2.5	Offer MRI-based planning for interstitial brachytherapy.	Unanimous support
Recommendations regarding scheduling		
2.6	Consider treating no more than 2 brachytherapy fractions per insertion.	Strongly supported

Topic 2 explanatory notes

Image-guided brachytherapy is considered the standard of care for the primary treatment of cervix cancer.[20]

Clinicians need to develop appropriate competency in the delivery of intracavitary brachytherapy. All specialist registrars should at least observe brachytherapy sessions with a range of complexities during training. Those interested in pursuing a career in gynae-oncology will require weekly scheduled hands-on training and should be encouraged to obtain a brachytherapy fellowship.

02

Topic 2: Brachytherapy

Integrating MRI into the imaging pathway is considered standard of care.[21]

MRI planning is defined as an MRI scan done on the day of procedure with an MRI-compatible brachytherapy applicator *in situ*. Images are used to mark gross tumour volume (GTV), high/intermediate-risk clinical target volume (HRCTV/IRCTV) and OAR and to calculate doses on planning software.[22]

Interstitial brachytherapy can be delivered using interstitial needles within an applicator (applicator interstitial)[23] or as a sole interstitial implant (template interstitial), usually delivered for gynaecological brachytherapy using a perineal template. If centres with applicator interstitial expertise do not offer template interstitial brachytherapy, they should develop links with a specialist centre where they can refer appropriate patients if required.

Complex brachytherapy is defined as:

- Procedures requiring interstitial insertions either with or without intracavitary applicators.
- Reirradiation using brachytherapy requiring non-protocol planning.

Indications for interstitial brachytherapy include:

- Large or wide residual GTV or HRCTV that would not be covered by intracavitary applicators only.
- Patients whose OAR dose would be reduced by use of interstitial needles.
- Vaginal, vulval or perineal disease extending into vaginal or paravaginal spaces.
- Complex pelvic recurrences such as vaginal vault disease that would not be covered with an intravaginal applicator alone.

Nationally, access to operating theatre time limits the ability to have multiple insertions for each patient. Use of 1 to 2 fractions per insertion may improve the patient experience and allows time for disease shrinkage between insertions, thereby decreasing cumulative OAR doses. However, it is recognised that some patients may prefer a single insertion for personal reasons, such as transport logistics, or social reasons.

03 Imaging and follow-up including late effects

Topic 3 statements

Statement		Voting outcome
Imaging following definitive radiotherapy		
3.1	Offer post-treatment imaging to assess radiological response and facilitate detection of salvageable recurrence if appropriate.	Unanimous support
3.2	Offer MRI at 3 months post treatment and consider positron emission tomography-computed tomography (PET-CT). Consider interval MRI imaging for cancer that is regressing but has not resolved at the 3-month scan.	Very strongly supported
3.3	Offer PET-CT if residual or progressive disease on MRI and a radical surgical option is available and appropriate.	Very strongly supported
3.4	For early detection of locoregional recurrence consider MRI of the pelvis, plus retroperitoneum if appropriate, at 1 year.	Strongly supported
3.5	For early detection of oligometastatic disease, offer CT imaging at 1 year and consider additional imaging beyond 1 year.	Strongly supported
Salvage surgery **Also refer to the reirradiation section (topic 4)**		
3.6	Consider salvage surgery by a specialist surgical team for histologically proven persistent or recurrent disease within the treatment field after definitive radiotherapy in order to achieve locoregional control, using the least morbid approach that will permit an R0 resection margin.	Very strongly supported
Late effects		
3.7	Offer pre-radiotherapy intervention to optimise health and minimise late effects, including smoking cessation and education on diet, hydration, physical activity, lifestyle factors, self-management tools and psychosocial support.	Unanimous support
3.8	Offer access to a comprehensive late effects service encompassing chronic pelvic pain, lymphoedema, menopause, mental health issues, sexual problems, and bone, dermatological, gastrointestinal, neurological or urological toxicity.	Unanimous support
Follow-up		
3.9	Consider personalised stratified follow-up based on risk of recurrence and toxicity. In selected patients this may include patient-initiated follow-up (PIFU) via a designated member of the MDT (eg specialist nurse or radiographer).	Very strongly supported
3.10	Ensure there is a well-defined pathway for patient access to rapid assessment in the event of suspected recurrence and/or development of late effects.	Unanimous support

03
Topic 3: Imaging

Topic 3 explanatory notes

The aim of follow-up after definitive cancer therapy is to detect recurrence, monitor and manage the late effects of treatment, collect data on outcomes, and support the physical and psychological needs of patients.

Imaging

In certain situations, there may be scope for radical salvage therapy, suggesting a role for radiological as well as clinical observation.

Imaging post treatment can be difficult to interpret. Current evidence suggests that following definitive radiotherapy, MRI at 3 months is the most useful means of assessing initial radiotherapy response, and PET-CT can be considered at 3 months, especially if the MRI result is indeterminate.[24–26]

For cervix cancer almost half of local recurrences in the EMBRACE-1 study were located in the lower vagina, likely to be identified on clinical examination.[27] The retroEMBRACE study showed that 85% of relapses occurred within the first 3 years and 95% within 5 years; 32% of patients had potentially salvageable (local, regional or para-aortic nodal) failure without systemic failure at first relapse.[28] The ongoing EMBRACE-II study performs MRI of the pelvis and retroperitoneum at 1 year.[14]

For high-risk cancer follow-up, there may be value in surveillance imaging to detect solitary and/or oligometastatic disease. How long surveillance imaging should be continued for is unknown and clinical studies would be encouraged in this area.

Well-designed observational studies and clinical trials to determine the potential benefit of rigorous and intensive imaging protocols on survival outcomes are required in order to guide practice.

Salvage surgery

Historical data show reasonable overall survival outcomes following pelvic exenteration for central recurrence of gynaecological cancers.[29–31] Advanced surgical techniques mean that surgery can be considered for previously inoperable cases, but obtaining an R0 resection margin remains a key critical factor.

Important prognostic indicators include:

- Negative nodes
- Absence of pelvic side-wall involvement
- R0 resection margin
- ≥12-month disease-free interval.

There is a lack of consensus on the role of surgery for persistent and recurrent disease <12 months following definitive chemoradiotherapy. The risk of grade ≥3 toxicity is high. Serial imaging is a reasonable alternative to surgery in the first instance to ensure true disease persistence rather than delayed response. Surgery should be reserved for highly selected patients after appropriate counselling. It is noted that in the EMBRACE-1 study some patients received serial scans up to 9 months before defining disease response.[27]

03
Topic 3: Imaging

- <12 months post definitive radiotherapy – be aware that persistent disease in the context of optimal treatment is a poor prognostic sign and surgery has no proven survival benefit, therefore very careful risk–benefit analysis should be performed.
- >12 months post definitive radiotherapy – large case series suggest a 40% 5-year overall survival, but careful risk–benefit analysis is still required in view of associated surgical morbidity.

A prospective database is recommended, and/or additional therapies such as immunotherapy require investigation.

Late effects

There is an increasing need to ensure equity of access to services that are specifically designed to minimise the burden of radiotherapy-related morbidity. Each centre should have access to a comprehensive late-effects service encompassing multiple specialists, but this is an area of significant unmet clinical need. An interim goal would be for a local radiographer or clinical nurse specialist (CNS) with a specialist interest. An ultimate goal would be a specialist service with access to multiple specialties, often at a regional or supraregional level.

The following categories of late effects are recognised:

1. Gastrointestinal
2. Urinary
3. Chronic pelvic pain
4. Sexual difficulties
5. Lymphoedema
6. Bone
7. Endocrine
8. Lumbar plexopathy
9. Vascular
10. Skin
11. Mental health and wellbeing

An increasing number of qualitative studies indicate poorer health-reported outcomes in patients with radiotherapy-related morbidity.[28,32]

Education on recognising the late effects of radiotherapy is essential for patients and healthcare professionals, especially as symptoms may develop years after treatment.

Prevention and education are key to minimising late effects. Introducing simple prehabilitation measures such as smoking cessation may reduce toxicity, improve tumour response rates and preclude the development of new malignancies.

Additional lifestyle measures such as hydration, nutrition and physical activity or pelvic floor training may contribute to longer-term health benefits.

Structured follow-up should always ask specifically about toxicity, and symptoms can be detected using screening tools. Investigation and interventions are often indicated.

The overarching Pelvic Radiation Disease Association Best Practice Pathway provides a benchmark for diagnosing and managing all of the sequelae of pelvic radiotherapy.[33]

Ultimately, appropriate infrastructure and funding should be agreed on a national level.

03

Topic 3: Imaging

Follow-up

Traditional follow-up schedules involve hospital visits for 5 years, and more frequently in the first 2 years when relapse rates are highest, primarily to detect asymptomatic recurrences that may be amenable to salvage treatment.[34,35]

These appointments can adversely impact mental health by causing anxiety and acting as reminders of diagnoses and can prevent symptomatic patients contacting clinical teams until their next visit. Also, there is no strong evidence that such an approach is cost-effective.[36,37]

Personalised stratified follow-up is a model of follow-up in which the clinical team and the patient make a decision about the best form of aftercare based on the individual's clinical and personalised needs.[38] PIFU is when a patient initiates an appointment when they need one, based on their symptoms and individual circumstances.

The British Gynaecological Cancer Society has published guidance on stratified follow-up, including PIFU.[39] The TOTEM trial in endometrial cancer has demonstrated that intensive follow-up schedules, although able to detect more recurrences, have no impact on overall survival when compared with 'minimalist' follow-up.[40] However, it is noted that 64% of recurrences were asymptomatic and that the 'minimalist' follow-up group still had regular clinical examination, just less frequently. The randomised OPAL trial of PIFU demonstrated significantly lower healthcare costs with a PIFU approach with no change in quality of life in patients with early endometrial cancer.[41] However, there were more primary care appointments and a greater fear of cancer recurrence with PIFU than hospital follow-up so the approach may not be preferred by all patients.

For PIFU there should be a clearly defined pathway, including initial holistic assessment, explanation of the process, information regarding symptomatology and a mechanism for rapid assessment in the event of suspected recurrence and/or development of late effects as part of PIFU. Some patients may be unsuitable for PIFU, for example if they have cognitive difficulties that may result in symptoms not being identified or reported.

PIFU can be adopted within the first 3 months following adjuvant (chemo)radiotherapy for intermediate-risk patients who have had brachytherapy.[42] However, high-intermediate and high-risk endometrial cancer patients who have had external beam radiotherapy are at a higher risk of late treatment effects and recurrences and therefore expert opinion suggests that these patients should be followed up for 2 years prior to adoption of PIFU.[16] It should be noted that patients need to be counselled about developing late side effects many years later and what potential late toxicity symptoms should initiate an appointment if on a PIFU pathway. Patient education is key and PIFU may be able to be initiated earlier in higher-risk patients if they are well informed and have a defined contact and pathway for review. Poorer endometrial cancer survival has been linked to economic deprivation and it must be ensured that the widespread introduction of PIFU does not contribute further to this.[43]

Literature on the use and efficacy of telephone review and/or PIFU in cervical, vaginal and vulval cancers is sparse. Patients with extensive field change due to intra-epithelial neoplasia and/or inflammatory conditions may benefit from regular clinical examination to minimise risk of further malignancy.

Patients with rare tumours will require an individualised follow-up protocol agreed at the MDT meeting.

04 Reirradiation of gynaecological cancers

Topic 4 statements

These statements should be used in conjunction with The Royal College of Radiologists principles of reirradiation guidance.[44]

Statement		Voting outcome
Imaging following definitive radiotherapy		
4.1	Offer multimodality imaging (using diffusion-weighted MRI, PET-CT and radiotherapy CT planning scan) to assess the extent of disease accurately.	Unanimous support
4.2	Consider reirradiation for isolated lymph node (LN) or pelvic soft tissue recurrence. Examples of suitable targets for a repeat course of radiation include: a. Oligometastatic pelvic LN relapse b. Oligometastatic soft tissue recurrences (eg vaginal vault, lower vagina, peritoneum) c. Unexpected positive margins following salvage surgery d. Palliation of recurrent pelvic disease.	Strongly supported
Quality assurance for reirradiation		
4.3	Review all reirradiation cases in MDT and peer review meetings. If not offered locally, cases should be discussed in centres that offer more advanced techniques such as stereotactic body radiotherapy (SBRT) and interstitial brachytherapy.	Unanimous support
Reirradiation technique		
4.4	Offer the most appropriate technique to adequately encompass disease and accommodate organ-at-risk (OAR) dose.	Unanimous support
4.5	Offer stereotactic radiotherapy for metachronous oligometastatic disease (<5–6 cm max dimension, OAR constraints achievable).	Very strongly supported
4.6	Consider interstitial brachytherapy for central pelvic or vaginal relapse.	Unanimous support
4.7	Consider VMAT or IMRT for palliative reirradiation cases.	Very strongly supported
Data collection for reirradiation		
4.8	Register all cases in any available national reirradiation audit and future national databases to inform further guidelines and the development of specific protocols or dosimetric constraints.	Unanimous support

04

Topic 4: Reirradiation

Topic 4 explanatory notes

All cases should be discussed in a multidisciplinary meeting regarding the appropriateness of reirradiation[45,46] and the most appropriate modalities such as surgery, stereotactic adaptive body radiotherapy (SABR) or brachytherapy.

Initial outcomes using image-guided brachytherapy and/or SBRT for reirradiation of gynaecological cancer are encouraging, with good local control and acceptable toxicity.[47–49] In general, central or low pelvic recurrences are amenable to reirradiation using brachytherapy whereas pelvic side-wall and extrapelvic recurrences are amenable to SBRT.

Targets for reirradiation should be reliably identifiable on MRI and/or PET-CT (in addition to planning CT). Intravenous contrast imaging may be helpful for difficult cases.

When using PET-CT, fluorodeoxyglucose (FDG) scans from skull base to femur can help detect small and distant metastases. When requesting a PET-CT scan, it should be made clear that imaging is to define the target and in addition to exclude small-volume metastases to ensure that offering treatment is appropriate.

Overlap with previous high-dose regions from brachytherapy (eg post cervix chemoradiation) should be carefully evaluated, and summation of all previous doses and evaluation of OAR tolerance and potential irradiated tissue recovery should be performed prior to any treatment planning. Reference should be made to the RCR reirradiation guidance for OAR tolerances.

It may be appropriate to offer reirradiation following surgery, for example if excision margins are unexpectedly positive following pelvic exenteration. The consensus group agreed that exenteration should always be carried out with the intention of complete excision of disease and that reirradiation in this setting should not be a planned procedure.

Generally, at least 6–12 months from previous irradiation should have lapsed before reirradiation.

All centres should have local expertise to deliver image-guided complex brachytherapy (interstitial) or, if not, a referral process should be in place to centres that do.

All centres delivering SBRT should demonstrate expertise in SBRT for reirradiation (eg registration via RTTQA or mentorship).

Routine prospective data collection is recommended to define optimal target doses and OAR dose constraints.

05 Molecular testing and sentinel lymph node assessment in endometrial cancer

Topic 5 statements

Statement		Voting outcome
Molecular testing		
5.1	Ensure access to immunohistochemistry or molecular testing for mismatch repair (MMR) (followed by hypermethylation testing where necessary) oestrogen receptors (ER) and p53 and next-generation DNA sequencing for POLE in all centres.	Unanimous support
5.2	All immunohistochemistry and/or molecular testing results should be available less than 6 weeks from diagnostic biopsy to ensure timely delivery of adjuvant therapy and enable trial recruitment.	Strongly supported
5.3	Offer adjuvant treatment based on a combination of pathology parameters including stage, histopathology and molecular classification	Very strongly supported
Sentinel nodes		
5.4	Offer sentinel nodal biopsy with ultra-staging with the purpose of guiding adjuvant therapy and sparing patients the morbidity of pelvic nodal dissection and combined modality treatment.	Very strongly supported
5.5	Collection of prospective data on outcomes and participation in clinical trials are encouraged.	Unanimous support

Topic 5 explanatory notes

Molecular testing will influence the clinical management of endometrial carcinoma.[50–53] Access to molecular testing for endometrial carcinoma is an essential tool for refining prognostic risk grouping and recruitment into clinical trials. Reference to current ESGO guidance is recommended.[16]

There has been limited access to POLE testing up to this point. Molecular POLE testing is now available at all genomic laboratory hubs (GLHs) in England as a part of the national genomic service.[54] All centres should implement this service.[55]

MMR testing can be done by immunohistochemistry or molecular analysis. GLHs can also perform molecular MMR or microsatellite instability (MSI) testing for all endometrial cancers, and pathology labs that do not have access to MMR immunohistochemistry can send samples to the GLH for molecular MMR or MSI analysis.[56]

05

Topic 5: Molecular testing

Molecular classification alone should not currently be used as the sole decision-making tool for adjuvant treatment until phase 3 clinical trial data are available. ESMO-ESGO guidelines are available[16] and outcomes from the PORTEC 4a and RAINBO studies will inform practice.

Further evidence is anticipated but current ESMO guidance suggests that adjuvant treatment could be omitted for POLE mutant stage 1 or 2 endometrial cancer and that chemotherapy should be considered in early stage (stage 1A myometrial invasion or stage 1B) p53 with no POLE mutation tumours.

Sentinel nodal dissection has increasingly become standard practice in many centres and is likely to result in fewer complications than systematic lymphadenectomy.[57,58] This is best performed using a laparoscopic or robotic approach. However, nodal sampling practice may begin to change in light of new molecular characterisation of endometrial cancer. Care needs to be taken to ensure that either a sentinel node dissection or a systematic lymphadenectomy will give new pathological information that may change the management of the patient. In some situations, a sentinel lymph node or a full systematic lymphadenectomy may well not change patient management. For example, a patient who has a p53 mutated tumour, POLE wild type, with >50% myometrial invasion would be recommended to have chemotherapy and external beam radiotherapy as they are high risk, so full systemic lymphadenectomy would not be recommended. However, currently the molecular classification is often not available prior to definitive surgery.

Acknowledgements

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Consensus participants

The following centres that deliver radiotherapy for gynaecological cancer were represented at the virtual RCR gynaecological cancer consensus meeting held on 13 September 2023.

Aberdeen Royal Infirmary	Oxford Cancer Centre, Churchill Hospital
Addenbrooke's Hospital	Peterborough City Hospital
Beatson West of Scotland Cancer Centre	Portsmouth Oncology Centre, Queen Alexandra Hospital
Belfast City Hospital	Queen Elizabeth Hospital
Bristol Haematology & Oncology Centre	Royal Derby Hospital
Castle Hill Hospital	Royal Devon & Exeter Hospital (Wonford)
Cheltenham General Hospital	Royal Marsden Hospital
Colchester General Hospital	Royal Preston Hospital
Derriford Hospital	Royal Surrey County Hospital
Dorset Cancer Centre, Poole Hospital	Royal Sussex County Hospital
Edinburgh Cancer Centre	Royal United Hospital Bath
Guy's and St Thomas' Cancer Centre	South West Wales Cancer Centre
Kent Oncology Centre	St Bartholomew's Hospital
Leeds Cancer Centre, St James' University Hospital	The Christie Hospital
Leicester Royal Infirmary	The Clatterbridge Cancer Centre
Lincoln County Hospital	The James Cook University Hospital
Musgrove Park Hospital	Torbay Hospital
New Cross Hospital	University College London Hospital
Norfolk and Norwich University Hospital	University Hospital Coventry & Warwickshire NHS Trust
Northampton General Hospital	University Hospital Southampton
Northern Centre for Cancer Care	Weston Park Hospital
Nottingham University Hospitals NHS Trust	Worcester Oncology Centre

We are also very grateful to patient representative Sarah Newman, founder of Get Me Back, who attended on the day to provide a patient perspective.

The first draft of the consensus statements was circulated to all of the UK cancer centres that deliver gynaecological cancer radiotherapy to discuss with their MDTs and to provide feedback. Feedback received was incorporated into the draft voted on at the 13 September 2023 consensus meeting.

Centres that provided written feedback on the statements prior to the 13 September meeting but which were unable to attend on the day:

Ipswich Hospital

Royal Berkshire Hospital

Royal Cornwall Hospital

Stakeholders

We are very grateful to the following stakeholder organisations that provided feedback on the first draft statements and/or provided a representative for the RCR gynaecological cancer consensus steering group:

British Gynaecological Cancer Society
Society and College of Radiographers
Institute of Physics and Engineering in Medicine
Royal College of Anaesthetists
Royal College of Pathologists
British Society of Urogenital Radiology
Pelvic Radiation Disease Association
Jo's Cervical Cancer Trust

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Abbreviations

3D	Three-dimensional
ACP	Advanced clinical practitioner
ART	Adaptive radiotherapy
CNS	Clinical nurse specialist
CO	Clinical oncology
CT	Computed tomography
DNA	Deoxyribose nucleic acid
ER	Oestrogen receptor
ESGO	European Society of Gynaecological Oncology
ESMO	European Society of Medical Oncology
ESP	European Society of Pathology
ESTRO	European Society for Radiotherapy and Oncology
FDG	Fluorodeoxyglucose
GLH	Genomic laboratory hub
GTV	Gross tumour volume
HRCTV	High-risk clinical target volume
IG	Image-guided
IMRT	Intensity modulated radiotherapy
IRCTV	Intermediate-risk target volume
ITV	Integrated target volume
LN	Lymph node
MDT	Multidisciplinary team
MMR	Mismatch repair
MRI	Magnetic resonance imaging
MSI	Microsatellite instability
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OAR	Organ at risk
PET	Positron emission tomography
PIFU	Patient-initiated follow-up
POLE	Polymerase epsilon
PRDA	Pelvic Radiation Disease Association
QA	Quality assurance
R0	Negative resection margins
RCR	The Royal College of Radiologists
RT	Radiotherapy
RTTQA	Radiotherapy trials quality assurance
SABR	Stereotactic adaptive body radiotherapy
SBRT	Stereotactic body radiotherapy
SIB	Simultaneous integrated boost
UK	United Kingdom
VMAT	Volumetric modulated arc therapy

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