

Sentinel Consensus Document for Vulval, Endometrial and Cervical Cancer BGCS January 2019

Christina Fotopoulou, Thomas Ind, Peter Baldwin, Robin Crawford, Omer Devaja, Stephen Dobbs, Jonathan Frost, Ketan Gajjar, Raji Ganesan, Sonali Kaushik, Jo Morrison, Marielle Nobbenhuis, Nithya Ratnavelu, Phil Rolland, Naveena Singh, Alexandra Taylor, Sudha Sundar, Andy Nordin

The BGCS officers and expert members of the UK gynaecological oncological community met to discuss evidence around the applicability, oncologic and surgical safety of the sentinel lymph node (SLN) technique in vulva, cervical and endometrial cancer and decide on their future implementation in UK gynaecological cancer centres. Full evidence of available studies and analyses was presented and discussed in detail among the experts, international guidelines were reviewed and taken into consideration, especially those of the European Society of Gynaecological Oncologists (ESGO).

A unanimous consensus could be reached for the SLN technique in vulva cancers as standard of care for specific tumours.

A Delphi process was applied to answer and reach consensus on critical key questions around the performance, technical aspects, training, sensitivity and specificity of the SLN technique, separately for cervical and endometrial cancers. Two rounds were required to reach consensus of $\geq 80\%$ in all points (including all strongly agree and agree responses).

We present here the consensus that was reached in the key questions of management and implementation.

Cervical cancer – Key consensus statements

1. When considering SLN in cervical cancer, women should be recruited to registered clinical trials.
2. Prospective and retrospective studies have demonstrated that SLN algorithms for surgical staging of cervical cancer have high Negative Predictive Values.

3. For women with cervical cancer where lymph node dissection is indicated, the use of SLN algorithms can be considered for surgical staging when imaging and clinical staging suggests that there are no metastases and Stage is Ia2 – Ib1, with a tumour size less than 2cm.
4. For women with cervical cancer Stage Ia1 with LVSI, the use of SLN algorithms can be considered for surgical staging.
5. The use of SLN algorithms compared to systematic lymphadenectomy in cervical cancer results in significantly less complications (including lymphoedema and lymphocysts).
6. The use of SLN algorithms in conjunction with systematic lymphadenectomy has a higher positive node rate than systematic lymphadenectomy alone.
7. When SLN algorithms are used in cervical cancer, a hemipelvis without a detectable SLN should have a full lymphadenectomy on that side.
8. A cervical injection of TC99 with dye or with ICG have emerged as better than blue dye alone in the detection of SLN in cervical cancer.
9. Histological ultra-staging protocols should be utilised in SLN algorithms for cervical cancer.
10. Surgeons who perform SLN mapping in cervical cancer should audit their outcomes including the overall detection rate, the detection rate for each hemi-pelvis, the bilateral detection rate, the presence of macro- metastases, the presence of micro-metastases, the presence of isolated tumour cells, the lymphoedema rate, the lymphocyst rate, complications and disease free survival.
11. The omission of a systematic lymphadenectomy in favour of SLN mapping in cervical cancer using histological ultra-staging and recourse to a full lymphadenectomy in unmapped cases, is acceptable in the management of cervical cancer patients if resources are available.
12. No consensus could be reached regarding the minimum number of cases needed for a typical learning curve for the SLN mapping technique in cervical cancer.
13. No consensus could be reached regarding the minimum case load needed to maintain skills in SLN mapping technique for someone who has already achieved the learning curve.

Endometrial Cancer – Key statements

1. Where possible and when considering SLN in endometrial cancer, women should be recruited to registered clinical trials.

2. Prospective and retrospective studies have demonstrated that SLN algorithms for surgical staging of endometrial cancer have high Negative Predictive Values.
3. For women with endometrial cancer where lymph node dissection is indicated, the use of SLN algorithms can be considered for surgical staging when imaging suggests that there are no metastases and there is no obvious extra-uterine disease at initial surgical inspection.
4. The use of SLN algorithms compared to systematic lymphadenectomy in endometrial cancer results in significantly less complications (including lymphoedema and lymphocysts).
5. The use of SLN algorithms in conjunction with systematic lymphadenectomy has a higher positive node rate than systematic lymphadenectomy alone.
6. A cervical injection of dye/tracer has emerged as the most suitable technique for SLN detection in endometrial cancer.
7. For SLN in endometrial cancer, either Indo-Cyanine Green (ICG) or a combination of blue dye and Tc99m labelled colloid have emerged as having higher reported detection rates than blue dyes alone.
8. Histological ultra-staging protocols should be utilised in SLN algorithms for endometrial cancer.
9. The omission of a systematic lymphadenectomy in favour of SLN mapping using histological ultra-staging and recourse to a full lymphadenectomy in unmapped cases, is acceptable in the management of endometrial cancer patients if resources are available.
10. Surgeons who perform SLN mapping in endometrial cancer should audit their outcomes including the overall detection rate, the detection rate for each hemi-pelvis, the bilateral detection rate, the presence of macro-metastases, the presence of micro-metastases, the presence of isolated tumour cells, the lymphoedema rate, the lymphocyst rate, complications and disease free survival.
11. Mapping SLN in endometrial cancer is best performed using a laparoscopic or robotic approach.
12. The use of SLN algorithms in endometrial cancer can be considered in women with high risk pathological types (e.g. clear cell, papillary serous, and carcinoma sarcoma).
13. When SLN algorithms are used in endometrial cancer, a hemipelvis without a detectable SLN should have a full lymphadenectomy on that side.
14. A typical case load for SLN mapping in endometrial cancer for someone who has already achieved the learning curve should be more than 10 cases/year.
15. No consensus could be reached regarding the minimum number of cases needed for a typical learning curve for the SLN mapping technique in endometrial cancer.

16. No consensus could be reached regarding the impact of obesity on the SLN detection rate.

Vulva Cancer – Key statements

1. Sentinel lymph node detection (SLND) using a combination of radioisotope and vital dye has a high nodal detection rate and is associated with high Negative Predictive Value (NPV) for early vulval cancer
2. SLN status is of prognostic importance
3. SLND without subsequent full lymph node dissection (LND) significantly reduces post-operative morbidity and hospital stay
4. There is a clear 'learning curve' associated with the surgical procedure and appropriate training is mandatory
5. For unifocal tumours <4cm without suspicious groin nodes on clinical examination and imaging, SLND is recommended as standard of care (providing appropriate expertise exists)
6. SLND is not associated with increased groin node recurrence rates when used in appropriately selected cases
7. The use of SLND in tumours >4cm is associated with reduced sensitivity and a higher groin node recurrence rate
8. The use of SLND for multifocal disease is associated with higher false negative rates
9. SLND is not recommended for large tumours >4cm; multifocal tumours; cases where representative injection is not possible; tumours that encroach on the vagina, urethra or anus; or where there is clinical or radiological evidence of metastatic disease
10. The node detection rate is far superior with radioisotope than with vital/blue dye and the use of a combination technique is associated with high sensitivity and low false negative rates
11. The use of radioisotope is essential based on current evidence
12. Alternative detection techniques such as fluorescence techniques with Indocyanine green do not yet have enough evidence for routine use in vulva cancer
13. SLND in recurrent disease is not yet well established and the standard of care for the groins remains inguinofemoral LND
14. SLND in obese patients may be associated with lower node detection rates but is not contraindicated in this group
15. The injection of the detection agents should be performed by an appropriately trained clinician with knowledge of both the tumour location and vulval anatomy

16. Intraoperative frozen section can be utilised in an attempt to avoid a second procedure but is associated with a high false negative rate. Caution is advised due to the potential loss of tissue for formal pathological assessment with the frozen section process
17. Ultrastaging with serial step sectioning and immunohistochemistry should be employed when the SLN is negative on routine H&E assessment
18. The combination of SLN detection with radioisotope followed by ultrastaging would appear to be a highly cost-effective strategy
19. When a SLN is not found, this is regarded as a ‘method failure’ and inguinofemoral LND should be performed.
20. For tumours involving the midline, bilateral SLN detection is mandatory. Where only a unilateral SLN is identified, this is regarded as ‘method failure’ and full inguinofemoral LND of the groin with SLND failure should be performed.
21. Where metastatic disease (of any size) is identified in the SLN, further treatment of the groin nodes is required. Current standard of care is ipsilateral inguinofemoral LND.
22. Follow up after SLND should be aimed at the early detection of nodal recurrence following a false negative SLND, as multimodal treatment may offer long-term survival in this group of patients.
23. Lymph node recurrence after SLND typically occurs in the first two years and the frequency of review during this time should reflect this fact.

Pathological processing and evaluation of SLN

Here, please refer to the document developed by the British Association of Gynae

Pathologists:

“Protocols for Pathological Processing of Sentinel Lymph Nodes in Endometrial, Vulval and Cervical Carcinomas” by Raji Ganesan, Ayoma Attygalle, Michael Coutts, Asma Faruqi, Mercedes Jimenez-Linan, W Glenn McCluggage, Brian Rous, Helen Stringfellow, Jonathan Williams, Naveena Singh.