

REVIEW ARTICLE

Precision Surgical Oncology through Artificial Intelligence Molecular Imaging and Biomarker Guided Therapeutic Strategies

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Keywords: Artificial intelligence; Precision surgery; Molecular imaging; Biomarkers.**How to cite this article:** Marowa chand (2026). Precision Surgical Oncology through Artificial Intelligence Molecular Imaging and Biomarker Guided Therapeutic Strategies, 3(3), 31-39.<https://doi.org/10.26524/amr.2026.3.4>**Abstract**

Surgery remains a major component of curative cancer treatment. Conventional surgical decision making is mainly based on anatomical imaging, histopathology, and clinicopathological features. These approaches have improved considerably but it cannot always identify microscopic disease. Recent advances in artificial intelligence, molecular imaging, and biomarker research are changing this situation. Molecular imaging provides surgeons with information about tumor biology during surgery through the use of targeted fluorescent probes and other imaging agents. Biomarkers such as circulating tumor DNA provide additional information about residual disease and the risk of recurrence after surgery. The combination of these technologies creates a new model of precision surgical oncology in which treatment decisions can be guided by both anatomical and molecular information. Artificial intelligence assisted hyperspectral imaging and Raman spectroscopy have demonstrated potential for intraoperative margin assessment in cancers. Circulating tumor DNA has further shown value in identifying patients at increased risk of recurrence after surgery and in selecting patients for adjuvant treatment. Despite these advances several limitations remain and most AI models require external validation. Molecular imaging agents remain target dependent. Biomarker assays require standardized methods and careful clinical interpretation. The integration of these technologies into routine surgical practice will therefore require prospective multicenter trials and appropriate regulatory frameworks. This review discusses the development of precision surgical oncology with particular emphasis on AI based decision to support biomarker guided treatment and future clinical translation.

1. Introduction

Cancer surgery has traditionally been guided by anatomical information. Surgeons use clinical examination and radiological imaging before surgery. During the procedure they rely on direct visualization and palpation. Histopathology is then used to confirm the diagnosis and evaluate the resection margins. This approach remains fundamental to cancer treatment. Meanwhile, the biological behavior of a tumor cannot always be determined from its anatomical appearance. Tumors are heterogeneous and malignant cells may differ within the same lesion. Some areas may show aggressive molecular characteristics while other regions may contain relatively less aggressive cells. Microscopic tumor deposits can also extend beyond the visible tumor boundary. These features create difficulties

during surgical resection. A surgeon may remove all visible disease while microscopic malignant cells remain at the resection margin. Such residual disease can contribute to local recurrence. The problem is particularly relevant in cancers where preservation of normal tissue is important. In brain tumors the problem becomes even more complex because excessive resection can cause neurological damage. Artificial intelligence has become an important component of this transition. AI systems can process large numbers of images and clinical variables. Machine learning can identify patterns within radiological images and digital pathology. Deep learning can classify tumor tissue and predict clinical outcomes. More recent approaches attempt to integrate imaging with genomic and clinical information. The AI applications now extend across imaging, biomarker

discovery, and surgical decision support (Figure 1 & Table 1). However, most studies still require larger external validation before routine clinical use (Chevalier et al., 2025; Hu et al., 2025; Selvaraj et al., 2025).

Molecular imaging adds another important dimension. Fluorescent probes can bind to tumor associated targets and make malignant tissue visible during surgery. This changes the role of imaging from a preoperative planning tool to an intraoperative decision support system. The clinical value of this concept has already been demonstrated in several tumor types. In malignant glioma surgery 5 aminolevulinic acid fluorescence increased complete resection of contrast enhancing tumor from 36% with conventional white light surgery to 65% in the fluorescence group. Six month progression free survival was also higher in the fluorescence group (Stummer et al., 2006). Biomarkers provide a third component of precision surgical oncology. Circulating tumor DNA is particularly important because it can identify molecular residual disease after apparently curative surgery. The DYNAMIC trial showed that ctDNA guided management in stage II colon cancer reduced the use of adjuvant chemotherapy without compromising recurrence outcomes. Five year recurrence free survival remained similar between the ctDNA guided and standard management groups (Tie et al., 2022, 2025). The combination of these approaches may allow surgeons and oncologists to move from anatomy based treatment toward biologically informed surgical care.

2. Artificial Intelligence in Precision Surgical Oncology

The first major contribution of AI to surgical oncology occurs before the operation. Modern cancer patients generate large amounts of information. This includes CT scans, MRI scans, PET images, pathology reports, laboratory results, genomic data and clinical records. Human interpretation of these datasets can be difficult when several variables must be considered at the same time. Machine learning models can identify relationships within these datasets. Radiomics is one important example and this methods convert medical images into quantitative features. These features may describe tumor shape, intensity, texture and spatial heterogeneity. Machine learning can then associate these features with tumor grade, molecular characteristics or treatment outcomes. This approach may be useful when tissue biopsy is difficult or when a single biopsy cannot represent the entire tumor. Imaging can provide information from a larger tumor volume. AI may therefore help identify regions that require additional sampling. Another important application is prediction of surgical difficulty. Tumor size and location are already used by surgeons. AI could add

information regarding vascular involvement, tissue planes and anatomical distortion. Such models may support selection of surgical approaches and help anticipate complications. AI can also assist multidisciplinary tumor boards. A recent systematic review of AI based clinical decision support systems in surgical oncology included 59 studies involving more than 23,000 patients. Reported agreement with multidisciplinary or guideline based recommendations varied widely from 23.2% to 99%. This variation shows both the potential and the current limitations of AI decision support (Wu et al., 2026).

Pathology remains the reference method for confirming malignancy. Digital pathology has created opportunities for computational analysis of whole slide images. AI algorithms can detect malignant cells and classify tissue patterns. They can also quantify features that are difficult to assess consistently by manual examination. The importance of this approach extends beyond diagnosis. Histological images contain information about tumor architecture and the surrounding microenvironment. AI models may identify features associated with prognosis or treatment response. Some models can also predict molecular alterations from routine histological images. Recent expert reviews from the European Society for Medical Oncology have highlighted the growing role of AI in tumor diagnosis and molecular biomarker detection. However clinical implementation remains dependent on robust validation and standardized pathology workflows (Marra et al., 2025). The integration of digital pathology with surgery could become particularly important for margin assessment. A rapid intraoperative imaging system could provide information about the resection margin before the operation is completed. This would allow the surgeon to remove additional tissue when necessary.

The operating room generates information continuously and video feeds show the surgical field. Imaging systems provide anatomical information and physiological monitors provide patient data. Computer vision is one of the most developed areas. Deep learning models can recognize surgical instruments and anatomical structures. They can also identify important surgical steps. In oncology this technology could eventually assist with tumor localization and identification of suspicious tissue. The current evidence is stronger for image interpretation than for autonomous surgical decision making. This is appropriate because surgical decisions often involve complex trade offs between oncological control and preservation of normal function. AI should therefore be considered as a decision support technology rather than a replacement for surgical expertise. The most useful

systems are likely to provide information at the moment when a clinical decision is required.

3. Molecular Imaging for Precision Cancer Surgery

3.1 Anatomical imaging to molecular imaging

Conventional CT and MRI provide detailed anatomical information. PET provides information about biological activity. However, many imaging methods do not directly identify the exact tumor boundary during surgery. Molecular imaging addresses this limitation by targeting specific biological features of malignant tissue. A molecular imaging probe generally contains two components. One component recognizes a tumor associated target. The second component produces a detectable signal. Fluorescent probes are particularly attractive because they can be visualized in real time. Near infrared imaging is widely investigated because tissue penetration is greater than with visible light. The technology can therefore provide information from tissue surfaces during an operation. Molecular imaging is particularly useful when the target is highly expressed by tumor cells. Heterogeneous expression can produce false negative areas. Normal tissues that express the same target can produce background fluorescence.

3.2 Fluorescence guided surgery

Fluorescence guided surgery is one of the most clinically advanced forms of molecular imaging. The surgeon receives an optical signal from the tumor while operating. This can reveal lesions that are difficult to identify with white light. The clinical evidence is strongest in several cancers. In malignant glioma the randomized phase III trial of 5 aminolevulinic acid demonstrated a substantial improvement in complete resection of contrast enhancing tumor. Complete resection was achieved in 65% of patients receiving 5 aminolevulinic acid compared with 36% in the white light group. Six month progression free survival was 41.0% versus 21.1% (Stummer et al., 2006). The value of this study extends beyond fluorescence itself. It demonstrated that an imaging technology can change the extent of cancer resection and influence an important clinical outcome. Ovarian cancer provides another important example. Pafolacianine targets folate receptor alpha. In a phase III study involving patients undergoing cytoreductive surgery, pafolacianine with near infrared imaging identified additional cancer in 33% of evaluable patients that had not been detected using white light and palpation (Tanyi et al., 2023). The US FDA review described pafolacianine as an optical imaging agent designed to identify malignant ovarian lesions during surgery. The agent binds folate receptor alpha and emits near infrared fluorescence after excitation.

3.3 Targeted imaging in prostate cancer

PSMA is another important target for molecular imaging. Prostate cancer cells frequently show increased PSMA expression. This has already been exploited for diagnostic PET imaging.

The same biological target can potentially be used for intraoperative fluorescence imaging. OTL78 is a PSMA targeted fluorescent tracer developed for this purpose. In a phase 2a first in patient study involving 18 patients undergoing robot assisted radical prostatectomy, OTL78 was well tolerated. PSMA targeted fluorescence allowed identification of visually occult prostate cancer and showed potential for improving complete oncological resection (Stibbe et al., 2023). A later phase II study evaluated OTL78 during pelvic lymph node dissection. This work further explored the ability of PSMA targeted fluorescence to detect lymph node metastases during surgery (Stibbe et al., 2025).

4. AI Enabled Intraoperative Imaging and Surgical Margin Assessment

The surgical margin is one of the most important determinants of local cancer control. A positive margin indicates that malignant cells are present at or close to the resection boundary. The problem is common in several solid tumors. Current intraoperative assessment relies on visual inspection and frozen section analysis. Frozen section provides useful information but requires tissue sampling. It also depends on pathology expertise and laboratory logistics. Sampling errors may occur when the tumor is large or heterogeneous. AI assisted optical imaging may provide a different approach. Instead of analyzing only selected areas the entire resection surface could potentially be assessed. Hyperspectral imaging captures information across multiple wavelengths. The resulting spectral pattern can distinguish tissues based on their optical properties. Machine learning can then classify the tissue. Early studies demonstrated the feasibility of this approach in breast cancer. In a study of fresh breast specimens from 18 patients more than 22,000 spectra were analyzed. A support vector machine was used for classification. Invasive carcinoma was correctly classified with 93% accuracy. The entire resection surface was imaged within approximately 10 minutes. HSI detected 19 of 20 malignancies located within 2 mm of the resection surface (Kho et al., 2019). Head and neck cancer is another important area. A study involving specimens from 102 patients investigated hyperspectral and autofluorescence imaging for detecting squamous cell carcinoma at surgical margins. Deep learning was used to analyze the images

(Halicek et al., 2019). More recently a study of head and neck squamous cell carcinoma used hyperspectral imaging together with convolutional and graph neural networks. The study included 32 patients. The combined approach achieved 86% accuracy for tumor tissue prediction in an ex vivo setting. The authors also identified data volume and imaging time as important barriers to clinical translation (Boehm et al., 2025). However, most studies remain ex vivo. The transition from specimen imaging to real time in vivo use requires faster acquisition and reliable image interpretation. Raman spectroscopy provides another label free method for tissue analysis. It measures molecular vibrations and produces a biochemical fingerprint of tissue. Cancerous tissue may show different molecular patterns compared with normal tissue. Raman spectroscopy has been investigated for several surgical applications. In oral cancer this technology has particular relevance because achieving an adequate surgical margin remains difficult. A 2023 study investigated Raman spectroscopy for intraoperative assessment of oral squamous cell carcinoma margins. The tissue classification model showed 85% sensitivity and 92% specificity. The margin prediction model showed a mean difference of -0.17 mm compared with histopathology (Aaboubout et al., 2023). A recent colorectal cancer study also demonstrated promising results. Raman analysis differentiated tumor margins from normal tissue with 82% classification accuracy. A portable system used immediately after surgery achieved 97% accuracy with 98% sensitivity and 96% specificity for cancerous versus healthy tissue classification (Karnachoriti et al., 2025). These results suggest that Raman spectroscopy could become useful for rapid tissue evaluation. AI may further improve its performance by converting complex spectral patterns into clinically interpretable classifications. Stimulated Raman histology represents another development. It provides rapid microscopic information without conventional tissue staining and AI can then classify the images. An initial clinical study of stimulated Raman histology included gliomas and other brain tumors. The AI assisted system achieved an AUC of 0.77 for tumor diagnosis. Prediction of IDH mutation showed an AUC of 0.93. Margin assessment showed correspondence with postoperative MRI in most evaluated cases (Nohman et al., 2024). The technology has also moved into prostate cancer surgery. Preliminary results from the ROBOSPEC study evaluated AI enhanced stimulated Raman histology during robot assisted radical prostatectomy. In the first 18 patients, the AI system showed sensitivity and negative predictive value of 1.0 at the patient level. The authors emphasized that the small sample size and single center design require further validation (Özkan et al., 2025).

The importance of these technologies lies in their ability to shorten the interval between tissue removal and biological interpretation. In future, this may allow the surgeons to modify the operation before leaving the operating room.

5. Biomarker Guided Surgical and Therapeutic Strategies

5.1 Tissue biomarkers

Molecular biomarkers can influence surgical planning before the operation. Genetic mutations and protein expression can provide information about tumor aggressiveness and treatment sensitivity. For example, HER2 expression influences treatment decisions in breast and gastric cancer. EGFR alterations are relevant in selected lung cancers. RAS mutations influence treatment selection in colorectal cancer (Hicks & Whitney-Miller, 2013; Linardou et al., 2008). These biomarkers are not just a diagnostic markers it can determine whether systemic therapy should be given before or after surgery. The concept of precision surgical oncology therefore extends beyond the operating room. Biomarker information can influence the timing of surgery and the need for neoadjuvant treatment.

5.2 Circulating tumor DNA

ctDNA has emerged as one of the most promising biomarkers for postoperative risk assessment. Tumor derived DNA fragments can be detected in blood. Persistent ctDNA after surgery may indicate molecular residual disease even when imaging shows no obvious tumor. The DYNAMIC trial provided important clinical evidence. Patients with stage II colon cancer were assigned to ctDNA guided treatment or conventional management. The ctDNA guided approach reduced the use of adjuvant chemotherapy without compromising recurrence outcomes. Five year recurrence free survival was 88% in the ctDNA guided group and 87% in the standard management group. The same study also showed that the amount of ctDNA detected after surgery has prognostic relevance. Patients with higher postoperative tumor derived mutant molecules had poorer recurrence free survival. ctDNA clearance during chemotherapy was also associated with favorable long term outcomes (Tie et al., 2025). These findings are important for surgical oncology because surgery alone cannot always determine whether the patient is cured. Molecular surveillance can provide an additional layer of information after resection.

5.3 ctDNA and treatment selection

ctDNA may also identify patients who require additional systemic treatment. The IMvigor010 study in muscle invasive urothelial carcinoma provided an important example. The overall trial did not demonstrate a benefit from

adjuvant atezolizumab. However, patients who were ctDNA positive showed worse outcomes with observation and appeared to benefit from atezolizumab. In the ctDNA positive subgroup the hazard ratio for disease free survival was 0.58. The hazard ratio for overall survival was 0.59 (Powles et al., 2021). More recent evidence has strengthened this concept. The phase III IMvigor011 trial evaluated ctDNA guided adjuvant atezolizumab in muscle invasive bladder cancer. Among ctDNA positive patients the median disease free survival was 9.9 months with atezolizumab compared with 4.8 months with placebo. Median overall survival was 32.8 months compared with 21.1 months (Powles et al., 2025). This is an important development in precision oncology. The decision for postoperative treatment can potentially be based on molecular residual disease rather than anatomical stage alone.

5.4 AI derived biomarkers

AI can expand the number of biomarkers available for clinical decision making. A model can combine imaging features with histology and molecular information. The resulting biomarker may be more informative than any single variable. A recent study using data from the IMvigor010 trial developed an AI based biomarker called UAIScore. The model integrated transcriptomic information with other biomarkers. High UAIScore was associated with better outcomes from adjuvant atezolizumab. The study also reported that UAIScore could provide information beyond ctDNA, tumor mutational burden and PD L1. Combining multiple biomarkers improved prediction further (Huang et al., 2025). This approach suggests that future surgical oncology will increasingly use composite biomarkers. Such biomarkers may combine clinical information with imaging and molecular features.

6. Clinical Applications Across Major Cancer Types

Head and neck cancer is an important setting for precision surgery. Local control depends strongly on complete tumor removal and positive margins increase the risk of recurrence. AI assisted hyperspectral imaging has shown potential for distinguishing tumor from normal tissue. Raman spectroscopy has also been investigated for intraoperative margin assessment. In oral cancer a Raman based model demonstrated 85% sensitivity and 92% specificity for distinguishing oral squamous cell carcinoma from healthy tissue (Aaboubout et al., 2023). These technologies may be particularly useful when tumor borders are difficult to define visually. Their clinical value will depend on faster acquisition and prospective intraoperative validation.

Brain tumor surgery provides a strong example of molecularly informed resection. The surgeon must remove as much tumor as possible while protecting functional brain tissue. 5 aminolevulinic acid has already demonstrated clinical benefit. The phase III trial showed higher complete resection rates and better six month progression free survival with fluorescence guided surgery (Stummer et al., 2006). AI based stimulated Raman histology is now being investigated as another tool. It could provide rapid information about tumor type and molecular characteristics during surgery. Initial clinical results suggest that prediction of IDH mutation may be possible using this approach (Nohman et al., 2024b).

Ovarian cancer often presents with extensive intraperitoneal disease. Complete cytoreduction is strongly associated with treatment outcome. Small lesions can be difficult to detect using conventional inspection. Pafolacianine provides a clinically advanced example of targeted fluorescence imaging. In the phase III study additional malignant lesions were detected in 33% of evaluable patients that were not identified using conventional white light and palpation (Tanyi et al., 2023). The technology demonstrates how a tumor associated receptor can be converted into a surgical imaging target.

Prostate cancer surgery is another field where molecular imaging may reduce the gap between oncological control and functional preservation. PSMA targeted fluorescence imaging has been tested with OTL78. The phase 2a study demonstrated feasibility and safety. The technology identified visually occult cancer during robot assisted radical prostatectomy (Stibbe et al., 2023). Future studies will need to determine whether better visualization translates into lower positive margin rates and improved long term biochemical control.

Colorectal cancer provides an important example of biomarker guided postoperative management. ctDNA can identify patients at high risk of recurrence after surgery. The DYNAMIC trial demonstrated that ctDNA guided treatment can reduce unnecessary chemotherapy while maintaining recurrence outcomes (Tie et al., 2022). Imaging based approaches are also being investigated for surgical guidance. Raman spectroscopy has shown promising accuracy in identifying colorectal tumor tissue and tumor margins (Karnachoriti et al., 2025). This combination illustrates how surgical precision and postoperative molecular monitoring can work together.

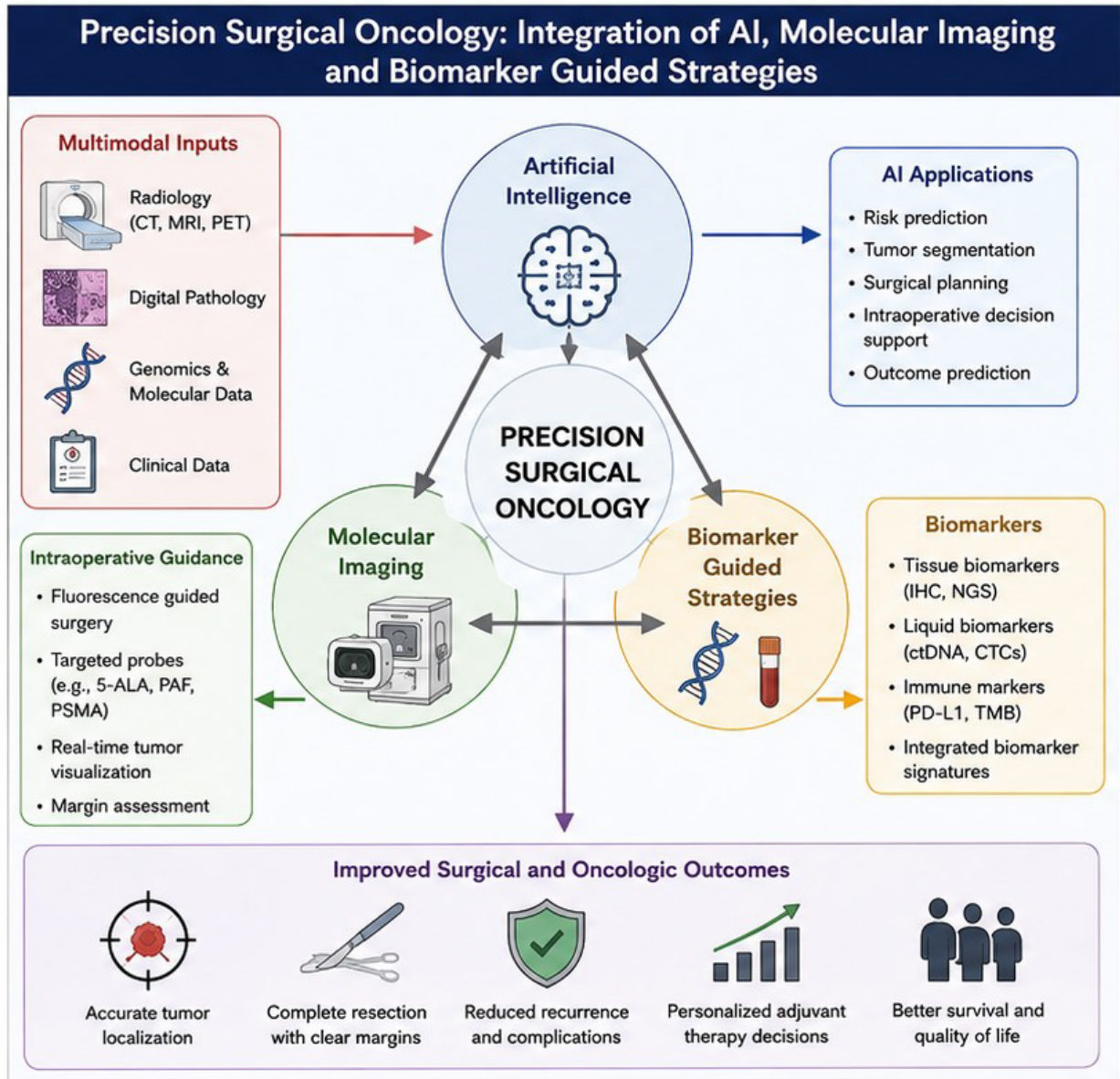


Figure 1: The precision surgical oncology includes the integration of artificial intelligence, molecular imaging, and biomarker guided strategies. These approaches support preoperative assessment, tumor localization, intraoperative guidance, margin evaluation, and postoperative monitoring. Their combined use may improve the completeness of tumor resection, support preservation of normal tissue, and guide individualized treatment decisions.

Table 1: Emerging technologies in precision surgical oncology

Technology	Surgical application	Key advantage	Major limitation	Reference
AI radiomics	Tumor characterization	Quantitative prediction of tumor features	Limited external validation	(Fanni et al., 2025; Xu et al., 2025)
Molecular fluorescence imaging	Tumor margin detection	Real-time visualization	Variable tracer uptake	(Lakomkin & Hadjipanayis, 2018; Rodriguez et al., 2025; Stummer et al., 2006)
5-ALA fluorescence	Glioma resection	Improved extent of resection	Incomplete fluorescence	(Rodriguez et al., 2025; Stummer et al., 2006)
AI computer vision	Intraoperative guidance	Real-time image interpretation	Dataset variability	(Cahill et al., 2025; Carstens et al., 2025)

AI-assisted robotics	Precision dissection	Improved surgical assistance	Limited autonomy	(Cahill et al., 2025; Xu et al., 2025)
3D surgical reconstruction	Surgical planning	Patient-specific anatomy	Tissue deformation	(Xu et al., 2025)
AI image fusion	Surgical navigation	Multimodal information	Registration errors	(Xu et al., 2025)
AI digital pathology	Margin assessment	Rapid tissue assessment	Requires validation	(Cahill et al., 2025; Xu et al., 2025)
Digital twins	Surgical simulation	Patient-specific prediction	High data requirements	(Xu et al., 2025)

7. Challenges Future Directions and Clinical Translation

Despite rapid progress precision surgical oncology remains at an early stage. The main challenge is the difference between technical performance and clinical benefit. An AI model may achieve high classification accuracy without improving patient survival. An imaging probe may detect additional lesions without demonstrating a reduction in recurrence. A biomarker may predict risk without reliably identifying patients who benefit from treatment. Meanwhile, AI also has several specific limitations. Training datasets may not represent the diversity of real world patients. Models developed at one institution may perform differently at another institution. Differences in scanners and imaging protocols can influence model performance. Pathology preparation can also affect digital image analysis. These issues make external validation essential. Surgeons and oncologists need to understand why a system has generated a particular recommendation. A black box prediction may be difficult to accept when the decision could alter the extent of surgery. Molecular imaging has a different set of limitations like the background fluorescence can complicate interpretation. Tumor heterogeneity may also reduce the sensitivity. Clinical adoption is therefore dependent on more than imaging performance. A useful system should be rapid and reproducible. It should be easy to interpret and should not significantly disrupt the operation. Biomarkers also require careful interpretation. ctDNA is a powerful example. A negative result does not necessarily mean that residual disease is absent. Tumor shedding varies between cancer types and between patients. Low tumor burden may produce ctDNA levels below the detection limit. Assay sensitivity and specificity therefore remain important. The economic dimension should also be considered. Precision technologies require imaging systems, molecular probes, and trained personnel. These requirements may limit access in resource constrained healthcare systems. Future studies should move toward prospective multicenter trials. These studies should evaluate clinical outcomes rather than only technical accuracy. The most useful future model is likely to be an integrated platform. Preoperative AI could estimate tumor

characteristics. Molecular imaging could identify malignant tissue during surgery. AI could assess the resection margin. ctDNA could monitor molecular residual disease. Biomarker results could then guide postoperative therapy. This approach could transform cancer surgery from a largely anatomy based procedure into a dynamic biological intervention. The priority should be to determine how these technologies can work together in real clinical workflows. Surgical oncology will benefit most when technology provides clear information at the moment of decision. The surgeon should remain responsible for the final treatment choice. AI and molecular technologies should provide additional evidence rather than replace clinical judgment.

8. Conclusion

The precision surgical oncology represents a developing model that connects artificial intelligence molecular imaging and biomarker guided therapy. The transition from promising technology to routine clinical practice will require rigorous validation and multidisciplinary collaboration. If these challenges are addressed precision surgical oncology may become an important component of individualized cancer treatment.

Declarations

Ethics approval statement

Not applicable

Consent to participate

Not applicable

Consent to publish

Not applicable

Data Availability Statement

The data are available from the corresponding author upon reasonable request

Competing Interests

The authors declare that they have no conflict of interest

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