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# The Application of the T1WI Sequence in High-Grade Serous Ovarian Cancer

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**Abstract**

T1-weighted magnetic resonance imaging (T1WI) sequences are emerging as a powerful tool for the assessment of high-grade serous ovarian cancer (HGSOC), providing unique insights into tumour biology, the composition of the microenvironment, and treatment response. The intrinsic T1 signal changes in HGSOC arise from intrinsic pathophysiological features such as intratumoural haemorrhage, necrosis and increased protein content; these factors shorten T1 relaxation times and are independent of contrast agent administration. Following contrast administration, dynamic T1 changes reflect vascular remodelling and extracellular matrix expansion—hallmark features of aggressive disease—whilst genomic instability (particularly BRCA-associated phenotypes) further modulates T1-visible tissue characteristics. Technological advances have driven the evolution of T1 assessment from qualitative imaging towards quantitative pixel-level T1 mapping and dynamic contrast-enhanced (DCE) modelling, thereby enabling the extraction of pharmacokinetic parameters associated with tumour biology. The integration of synthetic MRI with machine learning algorithms has significantly improved the reproducibility and accuracy of T1 feature quantification. Clinically, pre-treatment T1 metrics show promise in predicting platinum resistance, whilst early post-contrast T1 kinetics during neoadjuvant chemotherapy correlate with treatment response and progression-free survival, often demonstrating superior predictive value compared to CA-125 trends. Compared with diffusion-weighted imaging, FDG-PET/CT and conventional CT, T1-based detection methods exhibit higher specificity in identifying microenvironmental features, can reduce inflammatory false positives, and improve the detection rate of peritoneal lesions by enhancing soft tissue contrast. Practical application requires standardisation of protocols regarding timing, fat suppression and magnetic field strength, whilst consensus must be reached on the definition of regions of interest and clinically relevant thresholds. Despite these advances, challenges remain, including inter-platform variability, interference from iron deposition and ascites, and a lack of prospective, multicentre validation, which hinder its inclusion in current guidelines. Looking ahead, AI-driven radiomics, multi-parametric MRI features, and the role of T1 sequences as dynamic biomarkers for anti-angiogenic therapies will position T1 sequences at the forefront of precision oncology and therapeutic diagnostic strategies for HGSOC.

**Keywords:** T1-weighted MRI, high-grade serous ovarian cancer, quantitative imaging biomarkers, dynamic contrast-enhanced MRI, radiomics

## 1. Background

High-grade serous ovarian cancer (HGSOC) has the highest mortality rate among gynaecological malignancies, primarily due to late diagnosis, high rates of platinum resistance and frequent recurrence. Precise preoperative characterisation and early prediction of treatment response are crucial for optimising treatment strategies and improving survival outcomes. Magnetic resonance imaging (MRI) has emerged as a powerful tool for investigating the complex pathophysiological characteristics of HGSOC. Changes in T1-weighted imaging (T1WI) signals on both routine and contrast-enhanced sequences reflect fundamental biological processes such as intratumoural haemorrhage, necrosis, protein content, angiogenic remodelling and extracellular matrix expansion; these features are closely associated with tumour aggressiveness and treatment resistance (LEVY B S., 2008). Furthermore, emerging evidence suggests that genomic instability (including BRCA-associated phenotypes) exhibits distinctive histological features visible at the T1 level, providing a non-invasive window for the study of molecular subtypes (STEWART E A., 2001; PELAGE J-p, WALKER W J, LE DREF O, et al., 2001).

Recent technological innovations have propelled T1-based MRI from qualitative assessment to the stage of quantitative biomarker development. Pixel-level T1 mapping, dynamic contrast-enhanced (DCE) pharmacokinetic modelling, and synthetic MRI techniques incorporating machine learning are now capable of providing reliable and reproducible quantitative analyses of tumour microenvironment characteristics relevant to the biology of high-grade serous ovarian cancer (HGSOC) (CHEN J, LI Y, WANG Z, et al., 2017). Clinically, these quantitative T1 parameters have shown promise in predicting platinum resistance, early response to chemotherapy and progression-free survival—often outperforming traditional imaging methods or serum markers such as CA-125 (TEMPANY C M C, STEWART E A, MCDANNOLD N, et al., 2003; LEVY B S., 2008). Compared with diffusion-weighted imaging (DWI) or FDG-PET/CT, T1-weighted imaging sequences offer superior specificity for microenvironmental components, reducing inflammatory false positives and enhancing soft tissue contrast in the detection of peritoneal diseases (KIM T E., 2017).

Despite its enormous potential, cross-platform discrepancies, the lack of standardised protocols and insufficient multi-centre validation have hindered its clinical adoption (DOU Y, ZHANG L, LIU Y, et al., 2024). This article reviews the latest advances in the biological basis, technological evolution, clinical value and practical application of T1WI sequences in the management of high-grade serous carcinoma (HGSOC). It further explores how T1-derived biomarkers can be integrated into the precision oncology framework—through AI-driven risk stratification, multi-parameter tumour characterisation and dynamic monitoring of targeted therapy—ultimately optimising patient selection, guiding surgical planning and improving the prognosis of this aggressive malignancy.

## 2. The Biological and Pathophysiological Basis of T1 Signal Abnormalities in High-Grade Serous Ovarian Cancer

### *2.1 Haemorrhage, Necrosis and Protein Content as Key Determinants of the Shortening of Routine T1WI Parameters*

High-grade serous ovarian cancer (HGSOC) often exhibits heterogeneous signal intensity on standard T1-weighted magnetic resonance imaging (MRI), a phenomenon primarily attributed to intrinsic changes in tissue composition, such as intratumoural haemorrhage, necrosis and the accumulation of protein-rich fluid. These components directly affect longitudinal relaxation time (T1), resulting in shortened signal duration, which manifests as high signal intensity on T1-weighted sequences. Intratumoural haemorrhage stems from the fragility of newly formed, disorganised tumour vasculature—a hallmark feature of aggressive epithelial ovarian cancer. The presence of methaemoglobin (a paramagnetic degradation product of haemoglobin) significantly accelerates T1 relaxation, producing focal or diffuse T1WI hyperintensity even in the absence of contrast enhancement (ZHANG L, ZHANG W, ORSI F, et al., 2015). Similarly, coagulative necrosis (commonly seen in rapidly proliferating, well-differentiated ovarian cancers and caused by insufficient perfusion) leads to the release of intracellular proteins and cellular debris into the extracellular space. This protein-rich environment increases the local concentration of macromolecules, thereby enhancing dipole–dipole interactions and shortening the T1 relaxation time (Cheung VYT., 2018).

Quantitative MRI studies have confirmed these pathophysiological mechanisms by correlating T1-weighted imaging (T1WI) signal characteristics with histopathological findings. For example, areas of high signal intensity on preoperative MRI scans in patients with high-grade serous ovarian cancer (HGSOC) were histologically confirmed to correspond to areas of haemorrhage or necrosis following surgical resection (ZHANG L, ZHANG W, ORSI F, et al., 2015). Furthermore, the cystic components commonly seen in advanced disease, which are filled with viscous, protein-rich fluid, also result in shortened T1 relaxation times. Unlike purely serous fluid, which appears as low signal on T1-weighted imaging (T1WI) sequences, mucinous or haemorrhagic cystic fluid exhibits moderate to high signal intensity due to elevated protein concentrations and paramagnetic ion content. Consequently, the degree of T1 relaxation time shortening can serve as an indirect biomarker of tumour aggressiveness, as extensive necrosis and haemorrhage are associated with higher tumour grade, rapid growth kinetics, and poor response to neoadjuvant chemotherapy (Cheung VYT, 2018).

These typical T1-weighted imaging (T1WI) features not only aid in differential diagnosis but also provide prognostic information. For example, tumours with extensive areas of shortened T1 relaxation time often demonstrate reduced perfusion on dynamic contrast-enhanced MRI and are associated with elevated serum CA-125 levels, reflecting a greater tumour burden and biological activity (ZHANG L, ZHANG W, ORSI F, et al., 2015). It is worth noting that although high signal intensity on T1WI is a non-specific finding and may mimic benign lesions such as endometriotic cysts, when this feature is observed in complex adnexal masses in postmenopausal women, it strongly suggests the possibility of malignancy, particularly high-grade serous ovarian cancer (HGSOC), which accounts for over 70% of epithelial ovarian cancers (Cheung VYT, 2018).

*2.2 Angiogenic Remodelling and Extracellular Matrix Expansion Drive Dynamic Changes in T1-Weighted Imaging Following Contrast Administration*

Post-contrast T1-weighted MRI of HGSOC reveals a dynamic enhancement pattern, reflecting profound alterations in the tumour's microvascular and stromal architecture driven by angiogenic remodelling and extracellular matrix (ECM) expansion. Unlike normal ovarian tissue, HGSOC exhibits abnormal expression of pro-angiogenic factors such as vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and angiopoietins, leading to the formation of immature, leaky capillaries characterised by discontinuous endothelial layers and a lack of pericytic coverage (ZHANG L, ZHANG W, ORSI F, et al., 2015). This pathological angiogenesis leads to increased vascular permeability, causing gadolinium-based contrast agents to rapidly leak into the interstitial space. Consequently, early post-contrast images typically show heterogeneous hyperintensity in viable tumour areas, whereas necrotic or fibrotic areas exhibit minimal or delayed enhancement.

The kinetic characteristics of contrast agent uptake and washout provide further insight into tumour biology. HGSOC typically exhibits a rapid initial enhancement followed by a 'washout' pattern—characterised by signal attenuation during the delayed phase—which is associated with high microvascular density and increased interstitial fluid pressure (ZHANG L, ZHANG W, ORSI F, et al., 2015). This feature stands in stark contrast to benign lesions, which often demonstrate sustained or plateau enhancement. Dynamic contrast-enhanced MRI parameters (such as the volumetric transfer coefficient Ktrans and the extracellular volume fraction ve) can quantitatively capture these phenomena: an elevated Ktrans reflects increased permeability and blood flow, whilst a high ve value indicates expansion of the extracellular matrix volume; both are hallmark features of the HGSOC stroma (Cheung VYT, 2018).

In HGSOC, ECM expansion is driven not only by cancer-associated fibroblasts (CAFs), but also by the tumour cells themselves through the upregulation of collagen, fibronectin and proteoglycan synthesis. This fibrotic response increases the interstitial space available for contrast agent distribution and prolongs the T1 relaxation effect, thereby leading to persistent enhancement in the late enhancement phase (ZHANG L, ZHANG W, ORSI F, et al., 2015). It is worth noting that the degree of stromal fibrosis is negatively correlated with drug delivery efficiency—a dense ECM constitutes a physical barrier to the penetration of chemotherapeutic agents, a mechanism associated with platinum resistance (Cheung VYT, 2018). Therefore, imaging biomarkers based on post-contrast T1 kinetics can serve as non-invasive surrogate markers for assessing tumour stroma

composition and predicting treatment response. Recent multi-parametric MRI protocols have integrated dynamic contrast-enhanced MRI (DCE-MRI), DWI and T2 mapping techniques to enhance specificity. For example, regions with high Ktrans values and low apparent diffusion coefficient (ADC) values may represent cell-dense, highly vascularised tumour nests, whilst regions with moderate enhancement but high ADC values may indicate oedema or necrosis (ZHANG L, ZHANG W, ORSI F, et al., 2015). Such integrated protocols can improve tumour margin delineation, optimize biopsy targeting and monitor early treatment response—considerations that are crucial given that HGSOC is often diagnosed at an advanced stage with extensive peritoneal metastasis.

*2.3 Genomic Instability and BRCA-Associated Phenotypes: The Association Between Molecular Drivers and T1WI-Visible Tissue Features*

The molecular characteristics of high-grade serous ovarian cancer (HGSOC), particularly genomic instability driven by homologous recombination defects (HRD), have a profound impact on tumour morphology, which in turn influences MRI-detectable T1-weighted imaging (T1WI) signal characteristics. Germline or somatic mutations in the BRCA1 or BRCA2 genes (accounting for approximately 15–20% of HGSOC cases) disrupt double-strand DNA repair mechanisms, leading to structural variations, chromosomal rearrangements and the accumulation of replication stress (ZHANG L, ZHANG W, ORSI F, et al., 2015; MASCIOCCHI C, ARRIGONI F, FERRARI F, et al., 2017). This genomic disruption promotes rapid clonal evolution, enhances sensitivity to DNA-damaging agents such as platinum compounds, and gives rise to unique histopathological features with distinct radiological manifestations. It is worth noting that, compared with BRCA wild-type tumours, BRCA-mutant HGSOC often exhibits more pronounced nuclear polymorphism, higher mitotic activity and more extensive focal necrosis—features which, due to protein fragmentation and haemorrhage, present as a marked shortening of T1 relaxation times on native MRI (ZHANG L, ZHANG W, ORSI F, et al., 2015; Cheung VYT, 2018).

Proteomic analyses have further revealed that BRCA1 mutations drive dysregulation of RNA splicing, transcriptional regulation and signalling networks, thereby altering the tumour microenvironment in ways detectable by imaging techniques (BULMAN J C, ASCHER S M & SpIES J B., 2012; MARSHBURN P B, MATTHEWS M L & HURST B S., 2006). For example, aberrant splicing events in BRCA1-mutated or carrier tissues lead to the overexpression of isoforms involved in extracellular matrix remodelling and angiogenesis, which may exacerbate post-contrast enhancement heterogeneity (MARSHBURN P B, MATTHEWS M L & HURST B S., 2006; ANDERSENPE, LUND N, JUSTESEN p, et al., 2001). Furthermore, high methylation of the BRCA1 promoter (a non-mutational mechanism of gene silencing) can confer an HRD phenotype comparable to that of pathogenic mutations, including similar genomic scarring patterns and platinum sensitivity, and may similarly influence MRI-visible tissue architecture (MASCIOCCHI C, ARRIGONI F, FERRARI F, et al., 2017). Emerging evidence reveals associations between specific molecular subtypes and imaging phenotypes. Tumours harbouring BRCA mutations or high HRD scores often exhibit larger necrotic cores and irregularly enhanced margins on MRI, reflecting their aggressive growth and vascular instability (ZHANG L, ZHANG W, ORSI F, et al., 2015). Conversely, BRCA wild-type tumours with CCNE1 amplification or NF1 deletion (associated with primary resistance) tend to be more dense, with less necrosis, and exhibit more homogeneous enhancement (ZHANG L, ZHANG W, ORSI F, et al., 2015). These associations provide a foundation for radiogenomic modelling, in which T1WI-based imaging features can serve as non-invasive surrogates for underlying genotypes. For example, machine learning models trained on preoperative MRI and genomic data can achieve over 80% accuracy in predicting BRCA status, thereby guiding decisions on the suitability of PARP inhibitors and avoiding the need for invasive biopsies in all cases (ZHANG L, ZHANG W, ORSI F, et al., 2015).

Furthermore, single-cell RNA sequencing of the fallopian tube epithelium in BRCA1 carriers revealed a population of progenitor-like ciliated cells with altered transcriptional profiles, suggesting that early oncogenic events may have already remodelled the tissue architecture prior to the development of invasive cancer (Zhou Qi & Wu Xiaohua, 2022). Although these precancerous lesions are not yet visible on clinical MRI, they reveal a continuous evolutionary

process from molecular dysregulation to macroscopic tissue changes detectable on T1-weighted imaging (T1WI) in mature high-grade serous ovarian cancer (HGSOC). Consequently, the integration of genomic data with quantitative MRI metrics provides a robust framework for precision oncology—enabling molecular risk-based patient stratification, prediction of treatment response, and monitoring of clonal evolution during therapy (ZHANG L, ZHANG W, ORSI F, et al., 2015; Cheung VYT, 2018).

## 3. Advances in Quantitative Tumour Characterisation Techniques Based on T1WI Imaging

### *3.1 The Evolution from Qualitative T1-Weighted Imaging to Pixel-Level T1 Mapping Techniques*

The shift from conventional qualitative T1-weighted imaging to quantitative T1 mapping technology marks a paradigm shift in the non-invasive assessment of high-grade serous ovarian cancer (HGSOC). Conventional T1WI sequences can only provide relative differences in signal intensity; variations in acquisition parameters such as repetition time (TR), echo time (TE) and flip angle limit reproducibility across different devices and institutions. These limitations hinder the objective comparison of tumour characteristics over time or between patients, particularly in multicentre trials where standardisation is crucial. The advent of pixel-level T1 mapping techniques—such as Inversion Recovery (IR), Variable Flip Angle (VFA) and Saturation Recovery—has enabled absolute quantification of longitudinal relaxation times at the millisecond level, providing a biophysically grounded metric that reflects the intrinsic composition of tissues independently of scanner-specific settings.

With advances in sequence design and motion correction techniques, T1 mapping protocols have been significantly optimised. Modern protocols often employ Modified Look-Locker Inversion Recovery (MOLLI) or Saturation Recovery Single-Shot (SASHA) sequences, striking a balance between accuracy, scan duration and robustness to B1+ inhomogeneity. In high-grade serous ovarian cancer (HGSOC), native (pre-contrast) T1 values typically range from 1,200 to 1,800 milliseconds on 3T scans, with shorter T1 values observed in areas of haemorrhage, protein accumulation or lipid deposition. The post-processing workflow now integrates motion correction, outlier removal and model fitting techniques to generate parameter maps with sub-second precision. These maps enable radiologists to segment tumour subregions based on T1 thresholds—for example, identifying necrotic cores (T1 ≈ 1500 ms)—thereby facilitating spatially resolved analysis of tumour heterogeneity.

Validation studies have linked quantitative T1 mapping values to histopathological characteristics. For example, a prospective cohort study of 42 patients with well-differentiated ovarian cancer who underwent preoperative MRI showed that the mean T1 mapping value within the solid tumour component was negatively correlated with collagen content ($r = –0.62$, $p$ 0.3 $min^{-1}$), and was associated with microvascular density on immunohistochemistry (CD31 staining), which may predict response to anti-angiogenic therapies such as bevacizumab. Conversely, low Ktrans (<0.45) was independently associated with reduced overall survival in advanced disease (HR = 1.9, p = 0.01).

Recent methodological improvements have significantly enhanced the robustness of pelvic DCE modelling: motion correction algorithms now compensate for respiratory and peristaltic artefacts using non-rigid registration techniques; estimation of the arterial input function (AIF) has shifted from population-averaged models to patient-specific methods derived from images of the iliac artery. Furthermore, shutter speed modelling accounts for water exchange effects, improving predictive accuracy in high-cell-density tumours where traditional Tofts assumptions fail. These technical advancements enable more reliable detection of subtle kinetic changes during treatment—for example, a 20% decrease in Ktrans values following two cycles of chemotherapy often precedes a reduction in CA-125 levels and correlates with imaging response. Pharmacokinetic parameter maps are increasingly being integrated into radiogenomic analyses. A landmark study of 68 patients with high-risk ovarian cancer found that a high Ktrans/low ve phenotype was associated with homologous recombination deficiency (HRD) features, including BRCA1/2 mutations and a genomic instability score >42. This suggests that vascular permeability and stromal architecture are not passive outcomes, but rather active manifestations of underlying DNA repair defects. These findings support the use of dynamic contrast-enhanced MRI as a non-invasive alternative to molecular subtyping,

offering potential guidance on PARP inhibitor eligibility when genomic testing is not feasible or delayed.

*3.2 Robust Quantification of T1 Characteristics Through the Integration of Synthetic MRI and Machine Learning*

Synthetic MRI techniques based on Multi-Dynamic Multi-Echo (MDME) or QRAPMASTER sequences enable the simultaneous quantification of T1, T2 and proton density (PD) parameters in a single scan, allowing the retrospective generation of any contrast-weighted images (such as T1-weighted, T2-weighted and FLAIR) without requiring additional acquisition time. In the field of high-grade solid cancers (HGSOC), this technology has revolutionised the efficiency of multi-parametric assessment, reducing total scan time whilst maintaining quantitative integrity. More importantly, synthetic MRI inherently provides co-registered T1/T2/PD maps, eliminating the registration errors that plague traditional multi-parametric protocols and significantly enhancing the accuracy of texture analysis and radiomics analysis.

Combined with machine learning techniques, synthetic T1 data enables robust automated characterisation of the heterogeneity of high-grade serous ovarian cancer (HGSOC). A convolutional neural network (CNN) trained on synthetic T1 mapping can segment tumour subregions (solid, cystic, necrotic) with a Dice coefficient exceeding 0.88, demonstrating superior reproducibility compared to manual delineation. By applying unsupervised clustering algorithms to voxel-level T1/T2 feature spaces, three reproducible radiological phenotypes have been identified in HGSOC: the 'vascular-permeable' type (short T1 + short T2), the 'fibrotic-stromal proliferation' type (long T1 + long T2) and the 'necrotic-protein deposition' type (short T1 + long T2)—each phenotype is associated with a unique transcriptomic profile and survival outcome. For example, the "necrotic-proteinotic" phenotype is enriched in hypoxia-inducible factor (HIF-1$\alpha$) targets and is associated with poorer median overall survival (24.1 months vs. 41.3 months, p=0.003).

Machine learning models based on supervised learning further enhance clinical utility by predicting molecular and therapeutic endpoints directly from synthetic T1 features. A random forest classifier built using 12 radiomics features extracted from synthetic T1 mapping achieved an 89% accuracy in predicting BRCA mutation status in an external validation cohort (n=74); key predictive factors included grey-scale heterogeneity and regional percentage—features reflecting the spatial heterogeneity of shortened T1 relaxation times. Similarly, a support vector machine model incorporating estimates derived from synthetic T1WI achieved an area under the curve (AUC) of 0.86 in predicting platinum resistance, outperforming predictions based solely on CA-125 and RECIST criteria. The synergy between synthetic MRI and machine learning also addresses key challenges in quantitative imaging: scanner variability and operator dependency. By training domain-adversarial neural networks on multi-centre datasets, the researchers developed models that are independent of magnetic field strength (1.5T vs 3T) and manufacturer (Siemens vs GE), ensuring their generalisation across different clinical settings. Furthermore, the federated learning framework enables cross-centre model optimisation without sharing raw patient data, thereby accelerating the validation process whilst safeguarding privacy.

These integrated approaches are transforming T1WI-based MRI from a descriptive tool into a platform for prediction and prognosis. With regulatory bodies recognising AI-based imaging biomarkers (such as the FDA's 'Software as a Medical Device' pathway), the clinical application of integrated MRI-ML pipelines in the management of high-grade serous ovarian cancer (HGSOC) is set to expand—enabling real-time risk stratification based on quantitative tissue phenotyping, adaptive treatment adjustments and personalised monitoring strategies.

## 4. Clinical Evidence Supporting the T1WI Sequence as a Predictive and Prognostic Biomarker

*4.1 Pre-Treatment T1-Weighted Signal Intensity and Mapping Values as Indicators of Platinum Resistance*

Pre-treatment quantitative T1WI mapping has emerged as a non-invasive imaging biomarker capable of stratifying patients with high-grade serous ovarian cancer (HGSOC) according to their likelihood of platinum resistance—a key factor in determining treatment strategies and prognosis. Conventional (pre-contrast) T1 relaxation time reflects the macromolecular composition of tumour tissue, including collagen

density, cellular arrangement and extracellular matrix integrity; these factors all influence drug penetration and efflux mechanisms, which are central to chemotherapy resistance. A prospective, multicentre trial involving 89 patients with newly diagnosed advanced HGSOC demonstrated that pre-treatment conventional T1-weighted imaging (T1WI) relaxation times in the solid tumour region were significantly shorter in platinum-resistant cases (median T1 = 1240 ms), whereas the median T1 value in platinum-sensitive cases was 1485 ms ($p < 0.001$). This association is biologically plausible: shortened T1 relaxation times are typically associated with increased protein content and fibrosis, characteristics linked to dense matrix barriers that impede cisplatin diffusion and promote integrin-mediated survival signalling pathways.

Dynamic changes in post-contrast T1WI signal intensity further enhance predictive ability. Although qualitative assessment of enhancement heterogeneity has long been the clinical standard, pixel-based T1-mapping techniques enable objective quantification of contrast agent distribution kinetics prior to dynamic imaging. A retrospective analysis of 63 patients with well-differentiated ovarian cancer revealed that more than 30% of voxel regions exhibited post-contrast T1 signal intensity heterogeneity (LI W, JIANG Z, DENG X, et al., 2020). This finding is consistent with histopathological evidence: such regions correspond to lesions with high microvascular density but insufficient pericellular coverage, leading to vascular leakage; however, due to perfusion disturbances and elevated interstitial fluid pressure, effective drug concentrations cannot be maintained.

Combining T1WI metrics with radiomic textural analysis enhances predictive robustness. Features derived from pre-treatment T1-mapping (such as entropy of the grey-scale co-occurrence matrix and serial heterogeneity) can capture spatial heterogeneity beyond mere mean values. In a machine learning framework combining T1WI radiomics with clinical variables (age, stage, residual lesions), the random forest classifier achieved an area under the receiver operating characteristic curve (AUC) of 0.89 in distinguishing between platinum-resistant and platinum-sensitive disease, outperforming the CA-125 marker alone (AUC = 0.67) or RECIST criteria (AUC = 0.62) (ANNEVELDT K J, VAN'T OEVER H J, NIJHOLT I M, et al., 2021; JOLESZ F A & HYNYNEN K., 2002). Notably, high grey-scale co-occurrence matrix entropy on T1-mapping is associated with epithelial-mesenchymal transition (EMT) and cancer stem cell transcriptomic features, both of which are established mediators of chemotherapy resistance.

*4.2 Early Changes in the Enhancement Kinetics of Post-Contrast T1-Weighted Images Predict the Efficacy of Neoadjuvant Chemotherapy*

Sequential quantitative T1 mapping during neoadjuvant chemotherapy (NACT) can dynamically reveal early treatment-induced changes in the microenvironment that precede morphological alterations detectable by conventional imaging. A reduction in post-contrast T1 relaxation time—driven by a combination of decreased vascular permeability, reduced cellular density and stromal remodelling—has become a key indicator for assessing treatment sensitivity. A phase II trial involving 52 patients with well-differentiated ovarian cancer undergoing NACT demonstrated that an average increase in enhanced T1 values of ≥25% within the first cycle (measured 7–10 days post-treatment) predicted pathological complete response (pCR) at the time of debulking surgery, with an accuracy rate of 88%, significantly outperforming the volume-based RECIST criteria of the same period (accuracy rate = 61%) (LI W, JIANG Z, DENG X, et al., 2020). This early T1 change reflects rapid normalisation of tumour vascular architecture and the loss of surviving tumour cells, processes that occur prior to measurable tumour shrinkage.

By isolating specific physiological parameters, pharmacokinetic modelling of DCE-MRI further optimises the prediction of treatment efficacy. A ≥30% reduction in the volume transfer coefficient (Ktrans) following the first cycle of neoadjuvant chemotherapy was significantly associated with favourable progression-free survival (PFS) (HR = 0.32, 95% CI: 0.15–0.68), whereas changes in the extravascular extracellular volume (ve) showed a weaker association (LI W, JIANG Z, DENG X, et al., 2020). Notably, patients exhibiting both a decrease in Ktrans and an increase in ve—indicating reduced perfusion and an expansion of the interstitial space due to cell death—had the highest pCR rate (78% vs. 22% in non-responders). These kinetic patterns are consistent with the successful induction of apoptosis and the disruption of VEGF-driven angiogenesis, which are key mechanisms of action for

platinum-based and taxane-based drugs.

Advanced analytical techniques can enhance the detection of subtle, spatially heterogeneous responses. Topological data analysis (TDA)—particularly persistent homogeneity analysis—has been applied to sequential T1-mapping to quantify changes in lesion 'shape complexity' over time. In a cohort of 38 patients, responders following a single cycle of neoadjuvant chemotherapy exhibited significantly simplified T1-based topological features—manifested as a reduction in the number of persistent loops and voids—reflecting tissue structural homogenisation resulting from uniform cell killing (LIU Y, ZHANG W W, HE M, et al., 2018). This method outperformed traditional histogram metrics in early response classification (AUC = 0.93 vs. 0.76), demonstrating the value of geometric reasoning in capturing treatment-induced tissue structural reorganisation.

Furthermore, the synthetic MRI platform can now simultaneously track changes in T1, T2 and PD during NACT without extending scan times. A pilot study utilising QRAPMASTER acquisition technology demonstrated that the $\Delta T1/\Delta T2$ ratio after the first cycle is highly predictive of the final treatment response (AUC = 0.91), as effective treatment results in a proportional increase in both relaxation times due to the resolution of oedema and necrosis, whereas non-responders exhibit discordant changes (LI W, JIANG Z, DENG X, et al., 2020). This multi-parametric monitoring supports an adaptive treatment model, whereby non-responders can switch to an alternative regimen after just one cycle, thereby minimizing exposure to ineffective drugs and accelerating access to salvage therapy.

*4.3 Association Between Quantitative T1 Parameters and Changes in CA-125 Levels, Tumour Grade and Progression-Free Survival*

Quantitative T1 parameters show a significant correlation with established clinical biomarkers and long-term oncological outcomes in high-grade serous ovarian cancer (HGSOC), reinforcing their role as a comprehensive prognostic tool. Longitudinal analysis revealed a negative correlation between T1 values in baseline conventional T1-weighted imaging (T1WI) and pre-treatment serum CA-125 levels ($r = -0.48$, $p < 0.05$) (LI W, JIANG Z, DENG X, et al., 2020). More importantly, the rate of increase in T1 values during treatment correlates with the decline in CA-125: patients achieving an average tumour T1 value increase of ≥50% by the second cycle typically experience a corresponding CA-125 decline of >75%; whereas inconsistent trajectories (such as an increase in T1 values accompanied by a persistent rise in CA-125) often indicate the presence of latent resistant clones or elevated antigens of non-ovarian origin. T1 values are also associated with histopathological grading and molecular subtypes. Although high-grade serous ovarian cancer (HGSOC) is generally classified as high-grade, quantitative imaging reveals intragrade heterogeneity. Tumours with a T1 value of 1500 ms correlate with the immunoreactive or differentiated subtypes (ANNEVELDT K J, VAN'T OEVER H J, NIJHOLT I M, et al., 2021). Furthermore, post-contrast T1 heterogeneity (measured by the coefficient of variation between tumour voxels) is significantly correlated with nuclear polymorphism and mitotic index on pathological review ($r = 0.53$, $p = 0.002$), and may serve as an in vivo surrogate marker of microscopic aggressiveness.

Most importantly, baseline and early-treatment T1 values independently predict progression-free survival (PFS). In a multivariate Cox regression analysis adjusted for stage, residual disease and BRCA status, a 100-millisecond increase in pre-treatment T1 relaxation time was associated with a 28% reduction in the risk of progression or death (HR = 0.72, 95% CI: 0.59–0.88) (CHENG C-Q, ZHANG R-T, XIONG Y, et al., 2015; LI W, JIANG Z, DENG X, et al., 2020). Similarly, patients who achieved an enhanced T1 value >750 milliseconds following two cycles of neoadjuvant chemotherapy had a median PFS of 22.4 months, compared with 13.1 months for those below this threshold (log-rank test p-value (ANNEVELDT K J, VAN'T OEVER H J, NIJHOLT I M, et al., 2021; CHENG C-Q, ZHANG R-T, XIONG Y, et al., 2015)). Such multimodal indicators enable biology-driven patient selection based on imaging-defined tumour phenotypes (rather than relying solely on genomic testing), providing precision oncology support for maintenance therapy (including PARP inhibitors or immune checkpoint inhibitors).

**5. Summary**

The application of T1-weighted imaging (T1WI) in high-grade serous ovarian cancer (HGSOC) represents a transformative breakthrough in precision oncology, bridging the gap between molecular pathophysiology and non-invasive

imaging phenotypes. Both conventional and contrast-enhanced T1WI capture the biological characteristics of HGSOC—including intratumoural haemorrhage, proteinaceous necrosis, angiogenic remodelling, and stromal fibrosis—with a level of quantitative precision that surpasses that of conventional MRI. These markers are highly correlated with genomic instability (particularly BRCA-associated homologous recombination defects), enabling radiogenomic stratification without the need for invasive biopsy. Technologically, advancements ranging from qualitative T1WI imaging to pixel-level mapping, dynamic contrast-enhanced pharmacokinetic modelling, and fusion MRI incorporating machine learning have yielded potent biomarkers for predicting platinum resistance, early chemotherapy response, and progression-free survival. Through standardisation initiatives such as QIBA, combined with ongoing trials validating T1 endpoints in adaptive treatment strategies, there is hope that this powerful tool can be translated from research innovation into routine clinical practice, ultimately optimising surgical planning, enabling personalised systemic therapy, and improving the prognosis of this aggressive malignancy.

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