

1 **Field Cycling Imaging in ovarian cancer - a novel technology**

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3 Nanak Bhagat¹, Lionel Broche², Shylasree TS¹, Anne E. Kiltie³, Siladitya Bhattacharya⁴ and

4 Mahalakshmi Gurumurthy¹

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6 Affiliations:

7 1. Department of Gynaecological Oncology, Aberdeen Royal Infirmary, Aberdeen, United Kingdom

8 2. Aberdeen Biomedical Imaging Centre, School of Medicine Medical Sciences and Nutrition,
9 University of Aberdeen, Aberdeen, United Kingdom

10 3. Rowett Institute of Nutrition and Health, University of Aberdeen, Aberdeen, United Kingdom

11 4. School of Medicine and Dentistry, University of Aberdeen, Aberdeen, United Kingdom

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17 Author for correspondence:

18 Dr. Nanak Bhagat

19 Ward 315,

20 Department of Gynaecological Oncology

21 Aberdeen Royal Infirmary,

22 Aberdeen, AB25 2ZN

23 nanakbhagat@gmail.com

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32 **Commentary**

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34 Ovarian cancer causes more deaths than any other cancer of the female reproductive system
35 (1). Management of advanced high-grade serous ovarian cancers has relied on a combination
36 of effective chemotherapy and optimal debulking surgery which have been identified as key
37 prognostic factors.

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39 When optimal primary debulking surgery is not feasible in the presence of extensive
40 disease, neoadjuvant chemotherapy followed by interval debulking surgery is advocated.
41 The results of randomised trials have shown this approach to be associated with reduced
42 surgical morbidity and mortality with survival rates are similar to primary debulking
43 surgery.(2) . However, at the time of interval debulking surgery, areas where the disease has
44 responded to chemotherapy but has left thickened fibrotic unhealthy tissue present a major
45 challenge for surgeons. Uncertainty about the extent of tissue excised has led to variations
46 in care amongst surgeons, with some opting for extensive peritonectomy and visceral
47 resections with others choosing to undertake selective resection of areas where residual
48 disease is visible as fibrotic tissue. The presence of active tumour tissue in such areas is
49 often not obvious on inspection and can only be confirmed by histopathology, leading to
50 either extensive sampling or resection leading to increased surgical morbidity.

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52 In contrast to the stable magnetic field employed in most Nuclear Magnetic Resonance
53 spectrometers and Magnetic Resonance Imaging scanners, Field Cycling Imaging, a novel
54 technique developed at the University of Aberdeen, can discriminate between suspicious
55 areas *with* and *without* cancer by identifying differences in the interaction of altered water
56 and protein content in cancer cells. Field Cycling Imaging can generate rapid changes in the
57 magnetic field during a pulse sequence, thus allowing observers to study the behavior of
58 tissues over a range of magnetic strengths. Field cycling imaging results report nuclear
59 magnetic resonance dispersion profiles, a graphical representation of T_1 values (the
60 characteristic time taken for proton spins to reach their equilibrium state) plotted against the
61 strength of the magnetic field. T_1 is closely linked to molecular motion, offering an unique

62 opportunity to study molecular dynamics noninvasively (3,4) with variations in the T_1
63 dispersion curve linked directly with physical properties of tissues and cells (5).

64

65 To date, field cycling imaging work has shown promise in identifying the margins between
66 malignant and non-malignant tissue in women with breast cancer undergoing surgery (6),
67 and can potentially be utilised to differentiate active tumour from chemotherapy-induced
68 fibrosis in women with ovarian cancer.

69

70 This technology has the potential to change current practice in cancer detection, particularly
71 in treatment delivery and surgical planning. In the first instance we propose a pilot study to
72 assess the accuracy of field cycling imaging in identifying areas of active cancer in tissues of
73 women undergoing interval debulking surgery. These results could help us determine the
74 potential for further application of this technology in ovarian cancer.

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97 Authors response:

98 I confirm that I have not made any changes to the submission beyond those requested in this
99 decision letter. **[Yes]**

100 -All co-authors have reviewed and approved these changes. **[Yes]**