

## Significance of Second Near-Infrared Region (NIR-II) guided tumour detection and surgical treatment using Carcinoembryonic Antigen-Related Cell Adhesion Molecule (CEACAM) targetted probe in colorectal surgery

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Respected Ma'am, According to WHO, cancer alone killed 10 million people in 2018., making it a leading cause of mortality worldwide<sup>1</sup>. Near-infrared fluorescence-guided surgery, a rapidly evolving technique, enables surgeons to assess tumour borders of various cancer types and lesions of other prevalent illnesses with great precision. Near-Infrared Region (NIR) radiation's ability to absorb energy at one wavelength and emit it at a different, longer wavelength stimulates substances to fluorescence, aiding the complete surgical removal of tumour tissues with negative margins, thus, improving the disease's prognosis and decreasing chances of reoccurrence<sup>2</sup>. Conventional fluorescence-guided surgery focuses on the first near-infrared window (NIR-I, 700–900 nm), whose tissue penetration is limited to a depth of only 1-6 mm. In contrast, the second near-infrared window (NIR-II, 1000-1700 nm) significantly reduces tissue absorption, autofluorescence, and photon scattering, enabling a deep penetration (up to 20 mm), micron-scale resolution, and an increased tumor-to-normal tissue ratio (T/NT) leading to more precise tumour removal<sup>1-3</sup>.

A recent study in Beijing, China<sup>3</sup>, has explored the value of the second near-infrared window (NIR-II, 1000-1700 nm) in image guided surgeries that uses 2D5-IRDye800CW, as a targeted NIR-II probe formed by the conjugation of 2D5-CEACAM5 nanobody (2D5)<sup>34</sup> with IRDye800CW dye for intraoperative navigation in colorectal cancer which is the type of cancer known to have one of the highest mortality rates. To compare the efficacy of NIR-II with that of NIR-I comparative studies were also conducted on mouse CA colon, orthotopic cancer and metastasis models. Compared to NIR-I, NIR-II fluorescence had a much

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greater tumor to background ratio, the difference was statistically significant ( $p < 0.0001$ ) proving that the imaging probe was more sensitive in detecting tumours. This technique detected and resected tumours smaller than 2 mm, making it the most suitable option for cancer diagnosis and treatment<sup>3</sup>.

Henceforth, it can be deduced that 2D5-IRDye800CW and NIR-II fluorescence collectively have the potential to act as a way of improvement in surgery of colorectal cancer. Studies have also demonstrated the use of NIR-II systems for imaging the vasculature, detecting sentinel lymph nodes, image-guided cancer surgery, and fluorescence endoscopy<sup>4</sup>. Its other good attributes include high precision during image-guided procedures, over currently used NIR-I radiations<sup>3</sup>. Finally, NIR-II fluorescence technique's crucial role in detecting and treating tumours, highlights its importance and warrants further advancement.

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### Author's Contributions

**FM and HK:** Idea, conception, interpretation of the data,

literature review, analysis, drafting, editing, proofreading.