CORRESPONDENCE

Safety of Tattoos in Persons Undergoing MRI

TO THE EDITOR: Case reports of adverse reactions in persons undergoing magnetic resonance imaging (MRI) have implicated tattoos as a potential source of risk.[1-5] Quantitative data are lacking to inform the risk assessment of tattoo-associated adverse events among persons undergoing MRI, but these data are needed given the increasing prevalence of tattoos.

In a prospective study, volunteers at the University College London Wellcome Centre for Human Neuroimaging who were enrolled in neuroimaging studies involving scanners with a magnetic field strength of 3 Tesla were asked to participate if they had at least one tattoo and met specific inclusion criteria (≤5% of the body tattooed, tattoo or tattoos ≤20 cm in length, and no tattoos on the head, neck, or genitals) (see Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). The study was approved by the ethics committee of University College London, and written informed consent was obtained from all the participants.

Characteristics (the number, colors, and dimensions of the tattoos; the country in which the tattoos were applied; and the year of the application of the tattoos) were recorded along with the maximum specific absorption rate of the MRI sequences (which was maintained at <2 watts per kilogram) and the age and sex of the participants. The primary outcome measure was successful completion of MRI. If completion of MRI was unsuccessful, the event was deemed by the investigators to be an adverse reaction if it was tattoo-related.

Between 2011 and 2017, a total of 330 persons who were 18 to 66 years of age underwent MRI in a total of 585 sessions. Five different MRI scanners (one Allegra scanner, three types of Magnetom Trio scanners, and one Magnetom Prisma scanner, all manufactured by Siemens) had either a body coil (in 567 sessions) or a localized head coil (in 18) for radio-frequency transmission. Various types of functional and anatomical imaging were performed.

The participants had one to seven tattoos, and there were a total of 932 unique tattoos across the cohort. Black (in 717 tattoos) was the most common in a range of ink colors (Fig. S1a in the Supplementary Appendix). The maximum tattoo dimension ranged from 1.0 to 20.0 cm (Fig. S1b in the Supplementary Appendix). Tattoos were applied primarily in Europe (570 tattoos), the United Kingdom (456 tattoos), and the Americas (90 tattoos), as well as in Asia, Africa, and Australia. A total of 25 tattoos were applied by the participants themselves. The maximum specific absorption rate of the MRI ranged from 4 to 95%; the median rate was 36% (interquartile range, 29 to 44).

One participant retrospectively reported "awareness" of a tattoo and "tingling" when scanning began. This was not classified by the investigators as a tattoo-related adverse reaction, and it

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may have been prompted by instructions to the participant to monitor the tattoo location. Another participant, who had several tattoos, reported a warm and tight feeling around one tattoo on the wrist during the localizer sequence, and the MRI was terminated. This reaction was classified by the investigators as a mild tattoo-related adverse reaction. The sensation fully resolved spontaneously over 24 hours without medical intervention. No other tattoo-related adverse reactions were detected.

With the use of the Clopper–Pearson test, the estimated probability of an adverse reaction was 0.17% (95% confidence interval [CI], 0.00 to 0.95) assuming independent observations and 0.30% (95% CI, 0.01 to 1.68) assuming maximal correlation among repeated sessions for individual participants. Our findings indicate a low risk of tattoo-related adverse reactions under these specific study conditions.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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DOI: 10.1056/NEJMc1811197

CD47 Blockade and Rituximab in Non-Hodgkin's Lymphoma

TO THE EDITOR: Advani and colleagues (Nov. 1 issue)[1] report that the CD47-blocking antibody Hu5F9-G4 (hereafter, 5F9) had therapeutic efficacy in combination with rituximab in patients with lymphoma. On the basis of their preclinical studies,[2] the authors propose that 5F9 blocks CD47–SIRPα interactions and thereby improves tumor-cell phagocytosis by macrophages.

However, neutrophils (polymorphonuclear leukocytes) are the most numerous SIRPα-expressing effector cells, which trigger antibody-dependent cellular cytotoxicity of tumor cells by "frustrated phagocytosis" (i.e., neutrophils induce tumor-cell membrane disruption by repeated "biting"); this has recently been termed trogoptosis.[3] CD47 blockade enhanced polymorphonuclear leukocyte–mediated killing of solid-tumor cells by epidermal growth factor receptor antibodies of IgG isotypes.[4] However, rituximab did not recruit polymorphonuclear leukocytes for antibody-dependent cellular cytotoxicity against diffuse large B-cell lymphoma cell lines, whereas an IgA version of rituximab was effective. Since tumor infiltration by polymorphonuclear leukocytes often correlates with a worse prognosis,[5] we wonder what their contribution may be during 5F9 therapy.

Did the authors observe evidence that polymorphonuclear leukocytes positively or negatively affected the efficacy of 5F9 in their study? Addressing this issue may result in new approaches to enhance the efficacy of CD47 blockade.

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