Newly developed nanoparticles show promise for locating, removing endometriosis lesions

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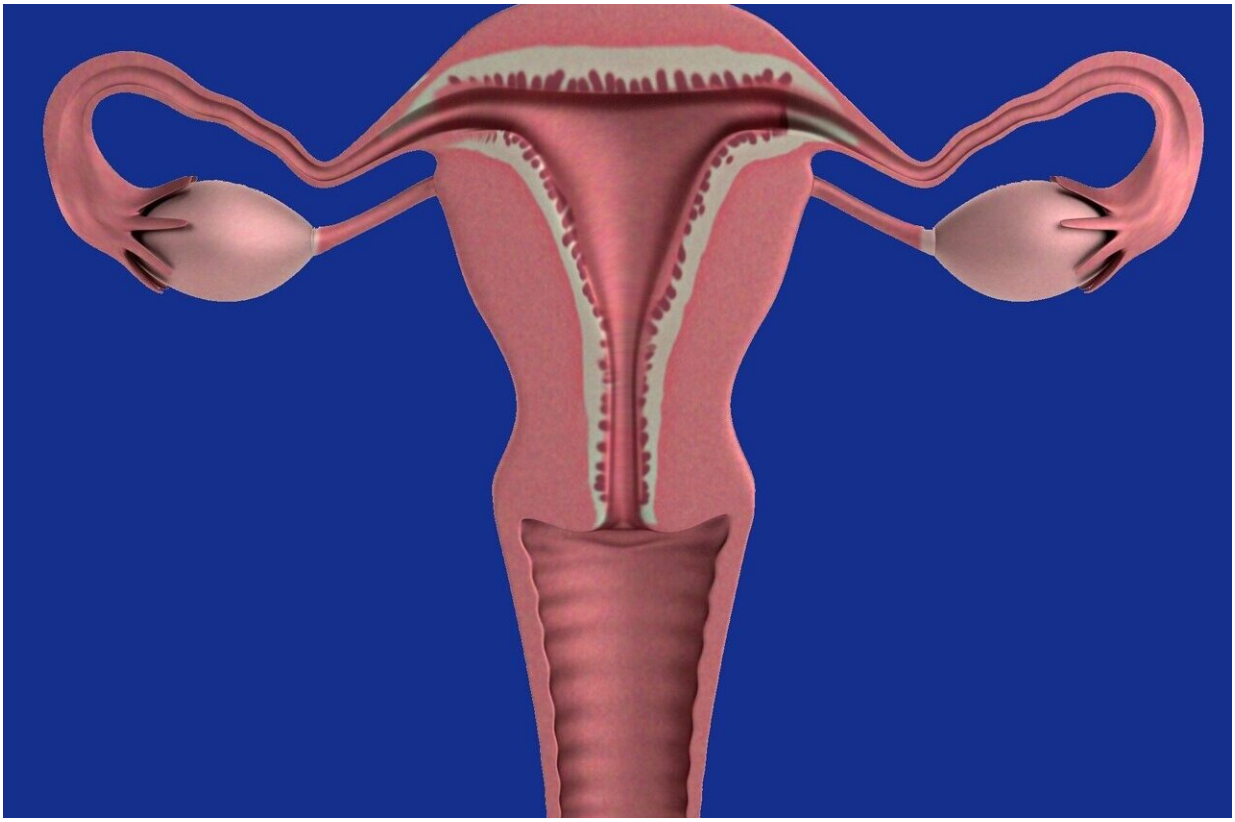

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Scientists have developed a new nanotechnology approach for locating and removing the painful and dangerous lesions associated with endometriosis, a common gynecological condition in women of

childbearing age.

The research led by Oleh Taratula of the Oregon State University College of Pharmacy and Ov Slayden of the Oregon National Primate Research Center at Oregon Health & Science University involves magnetic nanoparticles—tiny pieces of matter as small as one-billionth of a meter.

The animal-model study, published today in the journal *Small*, shows that the iron oxide nanoparticles, injected intravenously, act as a contrast agent—they accumulate in the lesions, making them easier to see by advanced imaging such as MRI.

And when exposed to an alternating magnetic field, a non-invasive procedure, the nanoparticles' temperature soars to more than 120 degrees Fahrenheit, high enough for lesion removal via heat.

"Endometriosis is a debilitating, systemic disease, and the need for an efficient, non-surgical method of removing the lesions is urgent," Taratula said. "We invented targeted nanoparticles with extraordinary heating capabilities that enable the use of magnetic hyperthermia for the safe and efficient elimination of endometriosis lesions."

The endometrium is the innermost layer of the uterus, and endometriosis occurs when endometrium-like tissue forms lesions outside of the uterine cavity—usually involving the ovaries, the fallopian tubes and the tissue lining the pelvis.

On rare occasions, endometrial tissue may spread beyond the pelvic region.

Roughly 10% of childbearing-age women will experience endometriosis, according to the World Health Organization, and 35% to 50% of women

with pelvic pain and or infertility suffer from the disorder. Globally, endometriosis affects about 190 million women, according to the WHO.

There's no cure for endometriosis, although surgical removal of the lesions can improve fertility. The downside, however, is that the lesions come back about half the time, and more than one-quarter of endometriosis surgery patients need three or more operations because it's hard to find all of the diseased tissue that needs to be removed.

"Endometriosis is a non-malignant condition, but the lesions sometimes perforate organs, resulting in a life-threatening situation," said Olena Taratula of the College of Pharmacy, who also collaborated on the study. "Therapies for pain result in infertility, and patients wishing to improve fertility often seek surgical removal of the lesions. And unfortunately, not only is the recurrence rate high, complications associated with surgery add to the overall risk."

Magnetic hyperthermia had not previously been considered as a potential means of ablating endometriosis lesions because other magnetic nanoparticles have relatively low heating efficiency, she said. The nanoparticles could only get hot enough after being directly injected into diseased tissue, which is not a realistic approach for endometriosis.

The collaboration that also included the College of Pharmacy's Youngrong Park, Abraham Moses, Peter Do and Ananiya Demessie overcame that problem by developing hexagonal-shaped nanoparticles that have more than six times the heating efficiency of conventional spherical nanoparticles when subjected to an alternating magnetic field.

Modifying the nanoparticles with a peptide—multiple amino acids linked in a chain—that targets a cellular receptor abundant in endometriosis cells enhanced their ability to accumulate in endometriosis lesions, the scientists said. Studies of mice with endometriotic tissue

transplanted from macaques demonstrated the nanoparticles' ability to eradicate the diseased cells following one session of magnetic hyperthermia.

"Furthermore, in collaboration with Khashayar Farsad from OHSU's Dotter Interventional Institute, we showed the efficiency of the same nanoparticles as an MRI contrast agent," Oleh Taratula said. "This feature of the nanoparticles can aid in the diagnosis of endometriotic lesions by MRI before their exposure to the external alternating magnetic field."

Also part of the project group were Addie Luo of the Oregon National Primate Research Center; Cory Wyatt of the OHSU Department of Diagnostic Radiology; Leonardo Campos and Younes Jahangiri of the Dotter Interventional Institute; Hassan Albarqi of Najran University in Saudi Arabia; and Parinaz Ghanbari, who helped prepare the graphical abstract illustrating the research.

More information: Youngrong Park et al, Targeted Nanoparticles with High Heating Efficiency for the Treatment of Endometriosis with Systemically Delivered Magnetic Hyperthermia, *Small* (2022). DOI: 10.1002/smll.202107808

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