INTERNET NEWS

BS. Nguyễn Văn Công

European Heart Journal

Volume 45, Issue 18
7 May 2024

JOURNAL ARTICLE EDITOR'S CHOICE

Low-dose colchicine for atherosclerosis: long-term safety FREE

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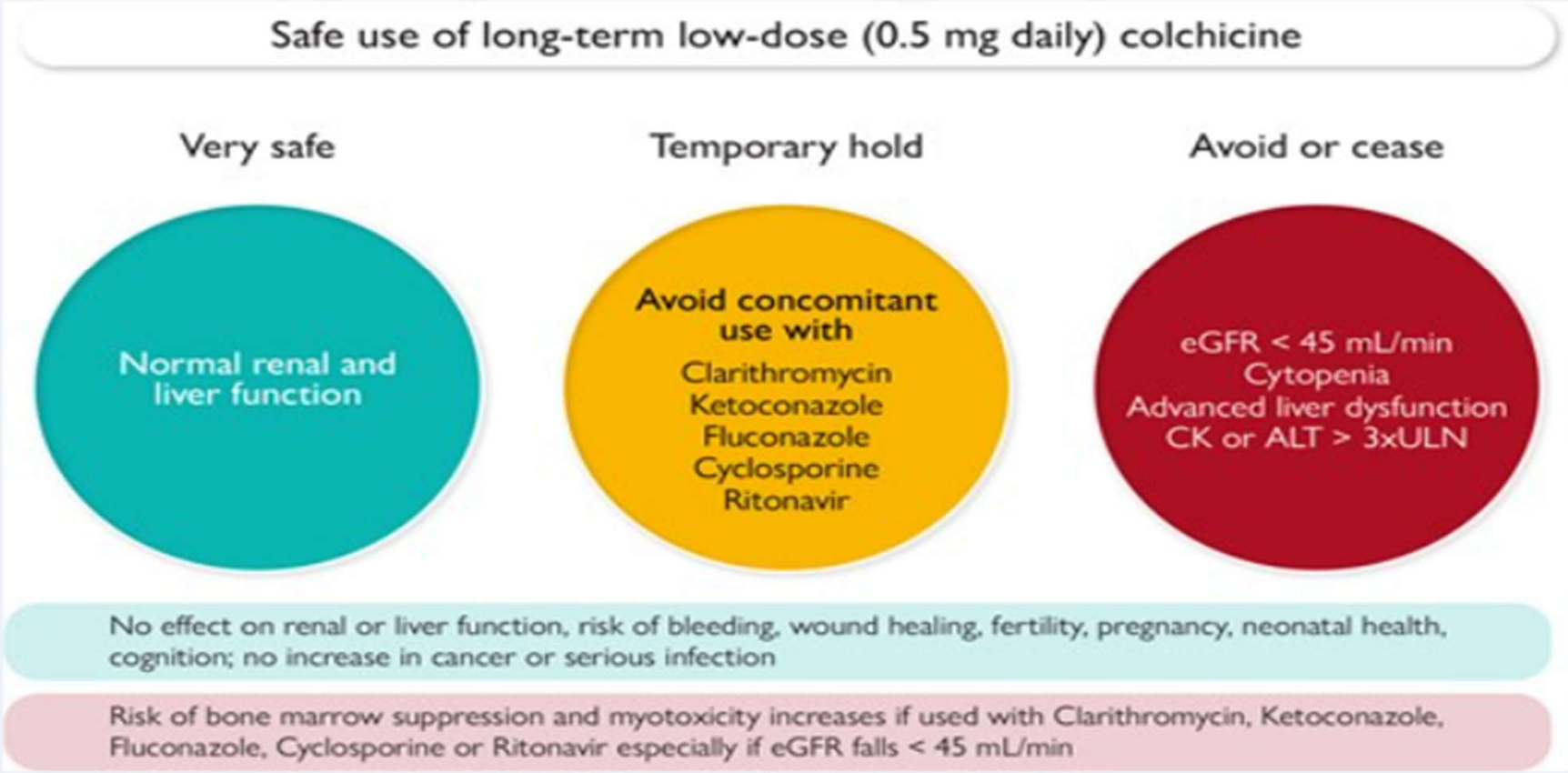
European Heart Journal, Volume 45, Issue 18, 7 May 2024, Pages 1596–1601,
https://doi.org/10.1093/eurheartj/ehae208
Published: 10 April 2024 **Article history** ▾

Abstract

Low-dose colchicine (0.5 mg daily) is now FDA-approved for secondary prevention in patients with coronary disease and will be increasingly prescribed in clinical practice. In this State-of-the-Art Review, data were collated from contemporary systemic reviews of case reports, drug registries, and placebo-controlled trials that assessed specific issues of safety related to the continuous use of colchicine in a range of clinical settings to inform physicians, pharmacists, and patients of the absolute risks of continuous use of low-dose colchicine, including among individuals taking statin therapy. Based upon these collective data, it is concluded that aside mild diarrhoea on initiation of colchicine that typically subsides in the vast majority of patients within a week of therapy, continuous use of low-dose colchicine is well tolerated and very safe. It does not affect renal, liver, or cognitive function, has no adverse effects on bleeding, wound healing, fertility, or pregnancy, and does not increase risks of cancer, serious infection, or cause-specific mortality. When appropriately prescribed to patients without significant renal or hepatic impairment, reports of myelosuppression, myotoxicity, and serious drug–drug interactions are rare and no more frequent than placebo, including in patients taking statin therapy. Physicians, pharmacists, and patients can be reassured that in the absence of significant renal or hepatic impairment continuous use of low-dose colchicine can be used safely in patients with atherosclerosis for the purpose of reducing cardiovascular risk.



Graphical Abstract Safe use of long-term low-dose (0.5mg daily) colchicine

Evidence Base

- Evidence was collated from systemic reviews of case reports, drug registries, and placebo-controlled trials published in the 20-year period between 2003 and 2023 related to the continuous use of colchicine in a variety of conditions. The aim of this review was to determine the effect of various therapeutic doses of colchicine on renal, liver, and cognitive function, bleeding, wound healing, fertility, and pregnancy, and the risk of cancer, serious infection, myelosuppression, myotoxicity, cause-specific mortality, and serious drug–drug interactions (DDIs). We also review safety data related to colchicine and myotoxicity when given as an adjunct to statin therapy, an issue raised in case reports where colchicine was inappropriately prescribed to individuals with renal or hepatic dysfunction but has not been seen in any of the contemporary clinical trials of statin-treated patients.

- **The effect of continuous colchicine use on liver function**
- Colchicine is also cleared by the liver and hence should be avoided in patients with significant liver disease. However, as will be reviewed here, colchicine itself has only modest effects on transaminase levels and does not initiate nor accelerate hepatic dysfunction.
- **Transaminitis**

Asymptomatic elevations in liver enzymes are commonly observed in practice. In patients with FMF, mild fluctuations in alanine transaminase (ALT) often settle without cessation of colchicine.[10,13] In patients with coronary disease, elevations in ALT $\leq 3 \times$ the upper limits of normal (ULN) are more common than placebo (colchicine 27.5% vs. placebo 17.4%). This does not appear to relate to the dose or choice of statin therapy. In contrast, elevations > 3× ULN are infrequent and no more common than placebo. Elevations in gamma-glutamyl transferase (GGT) are no more frequent in patients on colchicine (colchicine 16.0% vs. placebo 15.0%).[11] Thus, among patients with coronary disease, many of whom are diabetic, and most of whom are taking moderate or high-dose statins, transaminitis related to continuous low-dose colchicine is typically restricted to mild increases in ALT. In the setting of clinically significant transaminitis, especially if associated with a rise in GGT, colchicine should be temporarily discontinued and a comprehensive investigation of potential causes of liver dysfunction undertaken.

- **Hepatotoxicity**

There are two case reports in the literature of possible hepatoxicity associated with the use of continuous colchicine at 1 mg daily in the absence of sepsis, including one patient with chronic hepatitis C.[14] Though low-dose colchicine should not be given to those with significant hepatic disease, years-long controlled trials of colchicine at doses of 1 mg daily have generally proved safe in randomized trials of patients with alcoholic and biliary cirrhosis, albeit with limited clinical benefit.[15,16] A meta-analysis of 8659 patients randomized into placebo-controlled trials for a range of indications found that continuous therapeutic doses of colchicine at various doses were not associated with hepatotoxicity.[17] No evidence of hepatotoxicity was observed in either the LoDoCo2 or COLCOT trials in which virtually all participants were taking statin therapy.

- **The effect of continuous colchicine use on the risk of myotoxicity**
- Asymptomatic elevations in creatine-kinase (CK) and myalgia without a significant rise in CK are common in practice. However, myotoxic syndromes including subacute progressive muscular weakness and dysesthesia (myo-neuropathy), dysesthesia alone, or acute fulminating myalgia associated with weakness and marked elevation in CK (severe myositis or rhabdomyolysis) are very rare.
- Although the causes of myotoxicity are protean and a drug-related cause should be considered causal until proved otherwise, polypharmacy and co-existing morbidities often make it difficult to attribute the syndrome to a specific drug.[4,22] To date, evidence from the placebo-controlled trials of colchicine at doses varying from 0.5 to 2 mg daily indicates that the incidence of myotoxic syndromes is not increased in patients assigned colchicine.[12]
- **Bệnh lý cơ thần kinh**
- Trong một đánh giá có hệ thống về 143 trường hợp bệnh lý thần kinh cơ liên quan đến colchicine, hầu hết các trường hợp xuất hiện trong năm đầu tiên sử dụng colchicine liên tục ở những bệnh nhân dùng liều > 2,0 mg mỗi ngày. [24] Trong loạt nghiên cứu này, sáu trường hợp xảy ra ở những bệnh nhân dùng colchicine liều thấp để phòng ngừa cơn gút cấp, bao gồm ba người đã dùng thuốc này hơn 1 năm. Trong mỗi trường hợp, sự khởi phát liên quan đến các tác nhân kích hoạt có thể xác định được, bao gồm việc tăng liều colchicine tạm thời để điều trị cơn viêm cấp tính, việc sử dụng đồng thời các loại thuốc có khả năng tương tác mạnh với colchicine, hoặc suy giảm chức năng thận. Các triệu chứng lâm sàng thường thuyên giảm trong vòng vài tuần sau khi ngừng sử dụng colchicine. Trong loạt nghiên cứu này, 15 bệnh nhân mắc FMF đã được bắt đầu lại điều trị bằng colchicine với liều giảm mà không tái phát triệu chứng.
- **Bệnh lý thần kinh đơn độc**
- Mười hai trường hợp bệnh lý thần kinh đơn độc liên quan đến colchicine đã được báo cáo trong tài liệu. [24] Trong các thử nghiệm đối chứng giả dược, bệnh lý thần kinh ngoại biên rất hiếm gặp và không phổ biến hơn ở bệnh nhân dùng colchicine hoặc giả dược. [3 , 4 , 12]

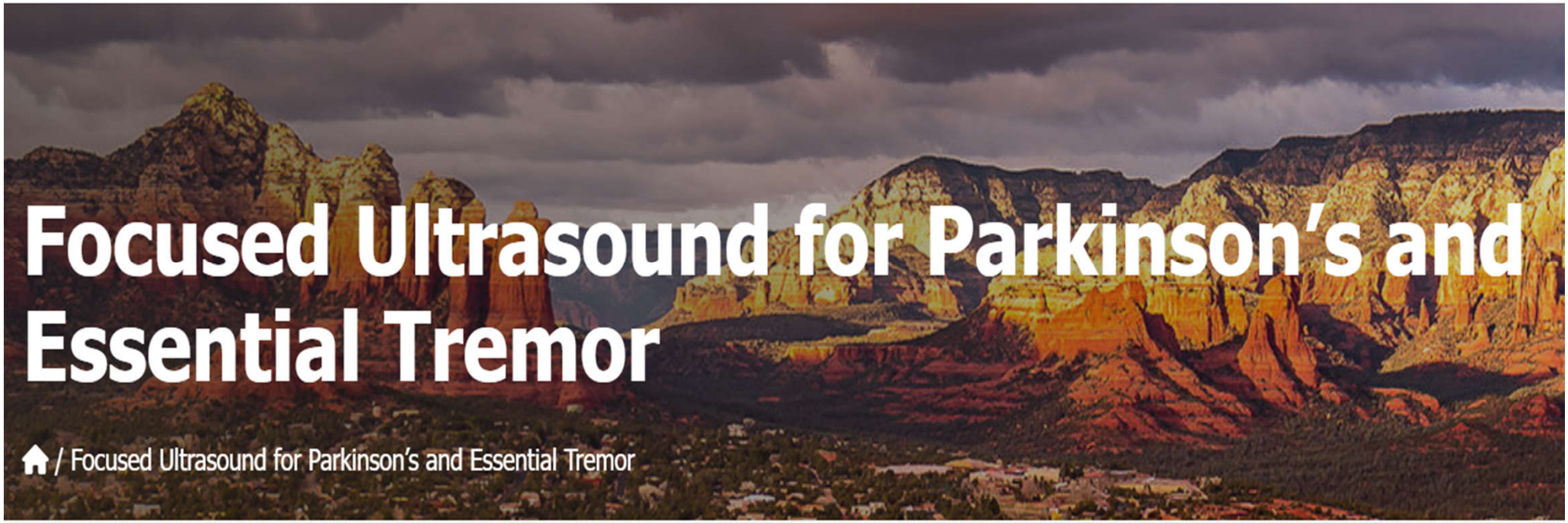
- **The effect of continuous colchicine use on the risk of infection**
- In a meta-analysis of all placebo-blinded randomized controlled trials conducted in a range of diseases in which colchicine was used at different doses and for variable lengths of time, there is minimal evidence that its use increases risks of serious or fatal infection.[17,31,32]
- In a retrospective cohort study of 131 565 patients with gout, the risk of non-fatal pneumonia was higher than among 252 763 matched controls over a mean follow-up of 6.7 years but was unrelated to colchicine use.[33] In a case-controlled study from Taiwan in patients with gout, the incidence of pneumonia was higher in patients treated with colchicine (ever-user 18.6 vs. non-user 12.6 per 1000 person-years), however, the risk was not related to the duration of therapy (<8 days: 1.33, 95% CI 1.20–1.48; 8–32 days: 1.45, 95% CI 1.31–1.60; >32 days: 1.47, 95% CI 1.33–1.62) suggesting that other factors may have been at play.[34]
- In the recent cardiovascular outcome trials, serious infections were uncommon. In the COLCOT trial, the incidence of pneumonia was low, albeit slightly more frequent in those assigned colchicine (colchicine 0.9% vs. placebo 0.4%, respectively, $P < .05$) but there was no difference in the overall risk of infection (colchicine 2.2% vs. 1.6% placebo).[4] In the LoDoCo2 trial, the rates of pneumonia and hospitalization for infection were low, and not different between treatment groups.[3]
- **The effects of continuous colchicine use on the risk of cancer**
- In patients with coronary disease followed out to 5 years, low-dose colchicine did not increase the incidence of all-cause cancer compared to placebo.[3,4] Evidence from registries with longer durations of follow-up suggests that colchicine if anything, may reduce the risk of cancer.
- In a study of almost 9000 patients with FMF followed for 40 years the incidence of cancer was lower than the general population.[35] In a subsequent study examining the incidence of cancer in 24 050 men with gout followed over more than a decade, the incidence of cancer was slightly higher than in 76 129 age-matched controls[36] (gout 6.68% vs. controls 6.43%, $P < .006$), however, the incidence of all-cause cancer, and in particular prostate and colorectal cancer, among ever-users of colchicine was significantly lower than in patients who never took colchicine (HR: 0.85, 95% CI: 0.77–0.94; $P < .001$). These observational findings are consistent with randomized placebo-controlled trial and data from the Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS) in which IL-1β inhibition significantly reduced rates of lung cancer in a dose-dependent manner.[37]

- **Effects of continuous colchicine on miscellaneous outcomes**
- **Platelet function, bleeding, and thrombosis**
- At therapeutic doses, colchicine interferes with leucocyte–platelet aggregation but not platelet–platelet aggregation.[38] Thus, colchicine does not augment the effect of anti-platelet therapies or enhance the risk of spontaneous or surgical bleeding. Although its effect on leucocyte–platelet interactions may contribute to the reduction of atherothrombotic events,[39,40] low-dose colchicine does not reduce the risk of deep vein thrombosis or pulmonary embolism.[3,4] In the contemporary LoDoCo2 and COLCOT trials, there was no increase in the risk of bleeding including among those taking concomitant anticoagulant and antithrombotic therapies.[3,4]
- **Gastrointestinal symptoms and intestinal bleeding**
- Mild diarrhoea commonly occurs soon after initiation of colchicine and is the major reason for cessation of therapy. However, it typically resolves with continued treatment and patients tolerant to low-dose colchicine after the first week rarely report late gastrointestinal intolerance.[3] Gastrointestinal bleeding related to continuous use of colchicine has rarely been reported. In the CLOKOA trial three patients taking colchicine 1 mg daily for osteoarthritis had gastrointestinal bleeding, however, patients were permitted to use NSAIDs during the trial.[41] In contrast, gastrointestinal bleeding has not been reported in patients with FMF or gout, nor among coronary disease patients despite wide use of concomitant antithrombotic and/or anticoagulant therapy.
- **Wound healing**
- High-dose colchicine can inhibit fibroblast mitosis, migration, and collagen deposition.[42] At 1 mg daily, colchicine does not slow the progression of biliary fibrosis or interstitial lung disease.[43,44] Therapeutic doses of colchicine do not impair wound healing.
- **Cognition**
- Two studies comparing cognitive performance using a variety of standard cognitive tests in 122 older patients on continuous colchicine for FMF with age–sex-matched controls found no evidence of a decline in cognitive function in those on colchicine.[45,46]
- **Male fertility**
- In healthy men, colchicine 1 mg daily over 4 months had no effect on sperm count, testosterone, follicle-stimulating hormone, luteinizing hormone, or prolactin levels.[47,48]

- **Pregnancy and breastfeeding**
- In mothers with FMF colchicine does not increase the risk of spontaneous abortion or foetal anomalies.[9,48] In breastfeeding mothers with FMF, neonates are exposed to levels of colchicine deemed safe.[49]
- **Cause-specific mortality**
- Meta-analyses of placebo-controlled trials confirm that colchicine does not increase the risk of death related to cancer, infection, or any other specific cause.[17] Among patients with FMF, continuous use of colchicine has been associated with a reduced risk of death related to renal failure,[50] and the life expectancy of patients compliant with colchicine has been found to match the general population.[51] In a meta-analysis of patients in contemporary cardiovascular trials, a non-significant reduction in cardiovascular mortality has been observed along with a small non-significant increase in non-cardiovascular deaths. However, in a careful review of these death events, no systemic pattern or cause-specific issues have been observed.[52]
- **Drug–drug interactions**
- Deaths related to colchicine toxicity are extremely rare and limited to wilful or inadvertent ingestion of very large quantities or inappropriate use at high doses in individuals with clinically significant renal and/or hepatic disease when given in conjunction with strong CYP3A4 inhibitors or P-gp inhibitors. The only fatal DDIs associated with colchicine related to the development of pancytopenia consequent to concomitant use with clarithromycin or cyclosporine at doses $\geq$ 1.5 mg daily.[19] There are scarce reports of DDIs associated with low-dose colchicine in patients with eGFR $\geq$ 45 mL/min/1.73 m^2, none of which were fatal.[5]

Conclusions

- Case reports related to serious adverse events including myelosuppression, myotoxicity, or death in patients taking colchicine highlight the need for care with its use, particularly at doses > 0.5 mg daily in patients with more than mild renal impairment or significant hepatic impairment in association with a few specific drugs.
- In contrast, data accrued from systemic reviews of case reports, drug registries, and meta-analyses of placebo-controlled trials indicate that in the absence of significant renal or hepatic impairment, serious adverse effects and DDIs in patients taking low-dose colchicine are very rare and no more frequent than placebo.[12] Thus, physicians, pharmacists, and patients can be reassured that in the absence of significant renal impairment (eGFR ≥ 45 mL/min/1.73 m^2) low-dose colchicine can be safely used in patients with coronary disease, including those taking statin therapy (*Graphical Abstract*).
- In keeping with guidelines related to the use of colchicine in patients with FMF,[10] patients with coronary disease on low-dose colchicine should have regular reviews to ensure compliance, to monitor the blood counts and renal function, and to permanently cease therapy if eGFR falls <45 mL/min/1.73 m^2 or cytopaenia develops. It is prudent therefore to monitor renal function when introducing or altering the dose of drugs that may lower eGFR, including diuretics, and angiotensin-converting enzyme inhibitors. Measurement of colchicine levels is not recommended. CK need only be checked in patients with myalgia or weakness, and all myotoxic drugs should be ceased if CK is >3× ULN until the cause has been determined. Low-dose colchicine should be temporarily discontinued during short-term treatment with clarithromycin, ketoconazole, fluconazole, cyclosporine, or ritonavir.[53,54]



Focused Ultrasound for Parkinson's and Essential Tremor

Overview

- Focused ultrasound thalamotomy describes the use of focused waves of sound to treat an area deep in your brain called the thalamus. This procedure can reduce or eliminate symptoms of essential tremor and can help with the tremor symptoms associated with Parkinson's disease.
- In focused ultrasound thalamotomy, sounds waves come from different directions and generate heat at the point where the waves converge. The heat ablates a portion of the thalamus. This prevents the firing of the circuits responsible for essential tremor, thus eliminating or reducing the tremor.

What is a thalamotomy?

- A thalamotomy is any procedure that ablates a part of the thalamus. In this context, an ablation refers to using heat for the intentional destruction of tissue for therapeutic purposes.
- Thalamotomies have been performed using various techniques for over 50 years to treat essential tremor and parkinsonian tremor. Techniques have included inserting a radiofrequency probe through a hole made in the skull, delivering focused radiation (similar to what is used for some tumors), and, more recently, focused ultrasound.
- Focused ultrasound thalamotomy does not require incisions or drilling of the scalp or skull. In addition, the sound waves do not have enough energy to cause damage except at the point where they converge. This means that portions of the brain more than a few millimeters from where the ultrasound is being targeted are not at risk of being damaged.

What is focused ultrasound thalamotomy used for?

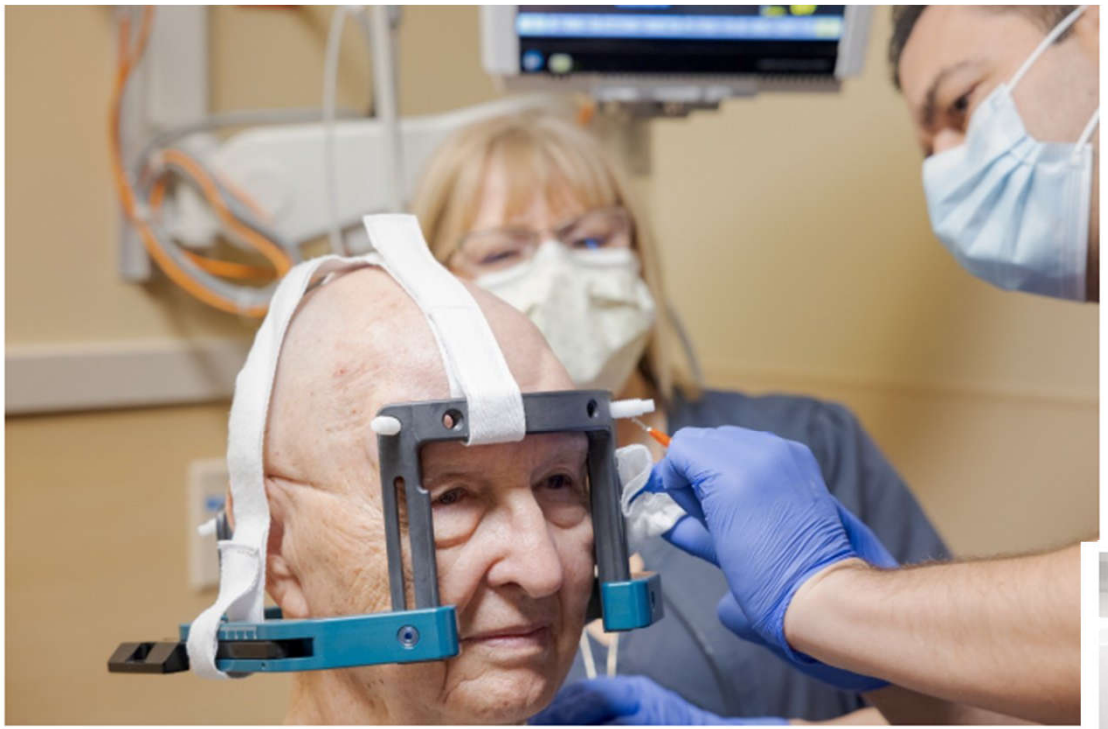
- Focused ultrasound thalamotomy is used to treat the following conditions:
- Essential tremor
- Parkinson’s tremor

Steps of Focused Ultrasound Treatment for Essential Tremor and Parkinson’s

- During this procedure, magnetic resonance imaging (MRI) is used to image the brain, guide the targeting of the ultrasonic waves, and monitor the temperature changes caused by the ultrasound energy.

MR images are used to plan and guide the delivery of the ultrasonic treatment.

It will be necessary to shave your scalp for this procedure to ensure that your hair does not interfere with the delivery of the sound waves.
Before the procedure, a stereotactic frame is attached to your head. This ensures that your head does not move during the MRI or as the sound waves are being transmitted. The frame is attached by pressure applied at four sites. Numbing medicine is injected to those four sites using a small needle. You will also take Tylenol, a steroid, and an anti-nausea medication before the procedure to control for symptoms during the procedure.



A patient with essential tremor receives numbing medication as the stereotactic head frame is placed on her head before the focused ultrasound procedure.

Because the sound waves can cause to you feel warm, our team will fit you with a cap that will be placed over your head like a headband. This will circulate cold water over your scalp to help you stay comfortable.

The patient is positioned and ready for the procedure to begin.

You will remain flat on the MRI table for the duration of the procedure, which lasts about two hours. The bed is padded for your comfort. The table will move in and out of the scanner as we image your brain, administer test doses to confirm therapeutic effect and evaluate for side effects, and administer the therapeutic doses.

Clinical staff monitor the patient as she receives focused ultrasound for essential tremor.

What to Expect: Side Effects and Recovery

Focused ultrasound thalamotomy is performed without any sedation, meaning you will be awake and alert during the procedure, including the placement of the headframe. Your neurosurgeon will ask you questions and have you perform tasks and movements to ensure the procedure is having the desired effect and to evaluate for side effects.

- This is an outpatient procedure, meaning you will go home on the same day as the procedure.
- Most people do not report pain during the procedure. Unsteadiness immediately after the procedure is common, and patients are recommended to take precautions not to fall. Many patients bring a walker, cane, or wheelchair to assist with balance after the procedure. Other symptoms may include dizziness, numbness, headache, nausea, or tingling. These effects usually are transient and improve with time.
- A short course of steroids is typically prescribed to help with side effects.
- There will be four points on your scalp where the pins from the frame were placed – above the eyebrows and behind the ears. Bandages and ointment will be placed on those areas. You may remove these and shower the day after.
- You are required to have a companion drive you home after the procedure. You may not drive for two weeks.

CLINICAL NEWS | WOMENS IMAGING

Critics slam Canadian breast screening guidelines

Amerigo Allegretto

May 31, 2024

Breast imaging organizations and political bodies are criticizing updated guidelines on breast cancer screening by the Canadian Task Force on Preventive Health Care (CTFPHC).

Released on May 30, the task force's draft guidelines recommend that women between the ages of 40 and 49 should not be systematically screened. Instead, these women are advised to have informed conversations with their primary care provider and make their own screening decisions from there. Additionally, the guidelines do not recommend supplemental imaging in women with dense breasts or women with a personal family history of breast cancer.

"There's so much misinformation out there, so we want women to be able to advocate for the screening they need, to know that breast cancer can happen at any age," said Jennie Dale, co-founder and executive director of Dense Breasts Canada. "We're hoping to get clear information out to women that they really have to look after themselves because with the state of confusion, it can be difficult."

Dense Breasts Canada is a nonprofit organization dedicated to raising awareness of breast density and advocating for best practices in breast cancer screening.

The CTFPHC's updated guidelines differ slightly from the guidelines issued by the U.S. Preventive Services Task Force (USPSTF) in April. The U.S. guidelines recommend biennial breast cancer screening for women ages 40 to 74, a grade B recommendation. The USPSTF also said that there was insufficient evidence to recommend supplemental screening with MRI or ultrasound in women, regardless of breast density.

These drew criticism from radiologic societies such as the American College of Radiology (ACR) and the Society of Breast Imaging (SBI), among others, which recommend annual screening starting at age 40 and with no age limit. The societies' guidelines recommend that women, especially Black and Ashkenazi Jewish women, receive a breast cancer risk workup by the age of 25.

Paula Gordon, MD, from the University of British Columbia, said that while the CTFPHC included observational studies, systematic reviews, and modeling in their decision-making for the updated guidance, the task force is "obsessed" with randomized controlled trials.

"So, when they looked at these outcomes, they gave greater weight to those 40- to 60-year-old randomized trials than to the modernized observational studies, said Gordon, who is also a volunteer medical adviser to Dense Breasts Canada.

Holland invited breast cancer experts to review the draft guidelines and share their critical analysis and called for the public consultation period from six weeks to a minimum of 60 days. He has also asked the Chief Public Health Officer to convene the senior provincial and territorial officials and key experts to review the guidelines and to share their best practices.

Holland also asked the Public Health Agency of Canada (PHAC) to advance the launch of an external expert review that will examine the CTFPHC's processes and provide recommendations to improve the task force's processes.

“It is important that Canadians trust the process of public health guidance. Public health guidance must protect Canadians,” Holland said. “That is why I am taking these actions today to make sure that Canadians have the resources they need to keep themselves and their loved ones safe and healthy.”

Dale said she hopes that Dense Breasts Canada will be able to work with Health Canada in these consultations.

“This is an issue that has the support of all the different parties in Canada,” she said. “We hope to work with everyone on it. It’s nonpartisan. They are all interested in the best screening for Canadian women.”

Gordon said that in the meantime, women in Canada should go to their doctor if necessary to get a requisition to have their mammograms “ideally every year,” or every two years if they live in a province that goes by biennial screening.

“If you’re in good health, keep having mammograms as long as you’re allowed to without a requisition, and then get a requisition,” she said. “There are loads of women in their early and mid-80s who are in excellent general health. If they get breast cancer, it would be best to find it early.”

IMAGING INFORMATICS | AI

AI reduces breast radiologist workload, false-positive cases

AI reduces breast radiologist workload while also improving screening performance and decreases the number of false-positive findings, according to a study published June 4 in *Radiology*.

A team led by Andreas Lauritzen, PhD, from the University of Copenhagen in Denmark found that the commercially available AI system used in a population-based mammography study led to a 20% decrease in the recall rate and a 33% decrease in reading workload.

"I think [AI] will add a lot of value to the radiologists themselves, where they have the tools and they can see markings from the AI," Lauritzen told *AuntMinnie.com*. "They can prioritize their time and resources to the cases that actually matter."

Retrospective studies have suggested that using AI can lessen the burden radiologists face when interpreting mammograms. Lauritzen and colleagues added that AI systems could serve as supportive tools for stratifying screenings based on breast cancer probability -- a possibility that has motivated exploration of their use in population-based breast cancer screening.

The researchers hypothesized that letting radiologists read mammograms with AI-assisted decision support and AI-provided lesion markings could increase screening sensitivity. They performed a study for which they compared workload and screening performance for two patient cohorts who underwent screening before and after the implementation of an AI system (Transpara v.1.7.1, ScreenPoint Medical).

The work included data collected between 2020 and 2023 from 60,751 women who underwent biennial screening before AI system implementation and 58,246 women who were screened after implementation. The women had a median screening interval before AI of 845 days and with AI of 993 days ($p < 0.001$).

Before AI system implementation (2020 to 2021), all screenings involved double reading. For screenings conducted after AI system implementation (2021 to 2022), "likely normal" screenings were single-read by one of 19 senior full-time breast radiologists.

The remaining screenings were read by two radiologists with AI-assisted decision support. Biopsy and surgical outcomes were retrieved between 2020 and 2023, ensuring at least 180 days of follow-up.

The team reported that the AI system implementation led to decreases in the recall rate, false-positive rate, and radiologist workload. It also reported increased cancer detection rate, positive predictive value, and the rate of small cancers.

AI implementation also led to the reading workload being reduced by 33.5% (38,977 of 116,492 reads).

The study authors wrote that future work should evaluate screening sensitivity, specificity, interval cancer rate, and the impact of higher ductal carcinoma in situ (DCIS) detection.

“Around November 2024, we will have full two-year follow-up data for the cohort of women screened with AI,” they wrote. “Further, in future work, we aim to quantify the effects of AI stratification, AI decision support, and radiologist access to prior screenings separately.”

Lauritzen said that the team doesn’t plan to implement other AI systems into their research.

In an accompanying editorial, Amie Lee, MD, from the University of California, San Francisco, and Sarah Friedewald, MD, from Northwestern University in Chicago wrote that the Lauritzen team’s study adds evidence to AI’s capabilities in breast imaging. However, they cautioned that implementing different versions of AI tools could lead to variable performance and that increased cancer detection alone is “not an acceptable proxy for the outcome of most interest, decreased mortality.”

“The types of cancers detected [tumor biology, size, grade, and node positivity] must be more rigorously studied,” Lee and Friedewald wrote. “Further studies are necessary to demonstrate the benefits of AI in other screening environments.”

CLINICAL NEWS | DIGITAL X-RAY

AI fracture detection device validated across three European hospitals

Will Morton
Aug 18, 2026

Article Summary

An AI fracture detection device called RBfracture demonstrated consistent performance across three European hospitals, with sensitivity ranging from 80-86% and specificity from 93-96%, while significantly improving clinician sensitivity by 11 percentage points when used as an assistive tool.

- RBfracture achieved **80-86% sensitivity and 93-96% specificity** across hospitals in Denmark, Germany, and the Netherlands
- AI assistance improved clinician sensitivity by **11 percentage points** while maintaining specificity
- Study analyzed **1,500 consecutive patient cases** (500 per hospital) aged 21 or older with suspected appendicular fractures
- Lower wrist and hand sensitivity (75% at one site versus 91-94% at others) suggests need for *anatomical subgroup optimization*
- Findings support broader clinical implementation pending workflow efficiency and patient outcome studies

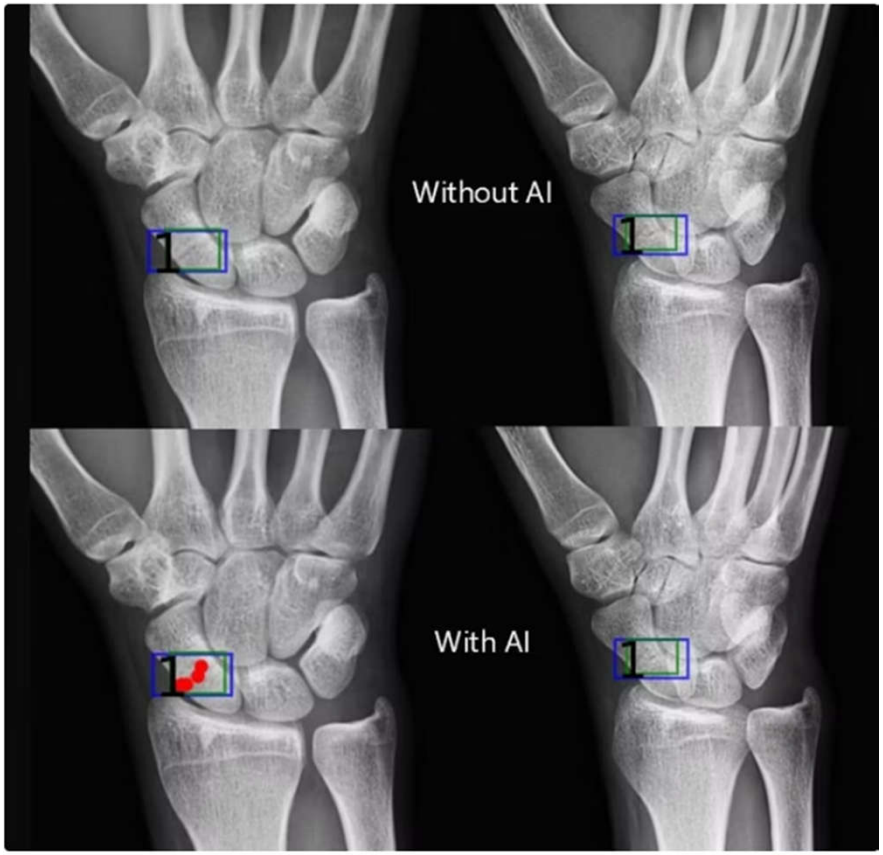
A commercially available AI device for detecting appendicular fractures showed consistent performance across three European hospitals and improved clinician sensitivity, according to a study published August 18 2026 in *Radiology*.

Led by a group at Erasmus MC University Medical Center in Rotterdam, the Netherlands, researchers evaluated RBfracture (Radiobotics, Copenhagen, Denmark), a CE-marked device for detecting extremity fractures on x-rays, with findings suggesting the tool generalizes robustly across health care systems and can benefit less experienced readers.

“Unlike curated or case-control datasets, we used consecutive cases, offering a more realistic assessment of the performance of the AI tool by capturing real-world conditions,” noted lead author Huibert Ruitenbeek, PhD, and colleagues. “Additionally, we validated the AI tool across datasets from different countries.”

Emergency department (ED) visits for acute fractures have been increasing globally, driven in part by the aging of the population, according to the authors. This increasing burden has placed significant demands on health care professionals and medical resources, they added. AI fracture detection tools have shown promise in improving diagnostic efficiency, but their performance across countries and health care settings and their effects on reader performance remain underexplored, the group wrote.

To approximate a “real-world” test of a device in this setting, the researchers use it to analyze x-rays of patients aged 21 or older with suspected appendicular fractures at academic medical centers in Denmark, Germany, and the Netherlands (n = 500 per hospital), collected consecutively between April 2018 to July 2022. In the multireader component of the study, 12 clinicians (four per site, spanning senior and junior radiologists and emergency physicians) evaluated 500 cases from their own institution with and without AI assistance.



Artificial intelligence (AI) assistance facilitates correct fracture identification in cases initially missed by human readers. A representative case is shown using anteroposterior radiographs in a 29-year-old male patient with wrist trauma (suspected nondisplaced transverse scaphoid fracture). The reader's initial unaided assessment (top) resulted in a missed fracture, whereas with AI assistance (bottom), the fracture was correctly identified. The green box represents the fracture location as predicted by the AI tool, the blue box represents the reference standard annotation, and the red dots represent individual reader annotations.

According to the findings, the hospital-level sensitivities of the AI tool ranged from 400 of 500 (80%) to 430 of 500 (86%) and specificities ranged from 465 of 500 (93%) to 480 of 500 (96%). An anatomy-based subgroup analysis revealed lower sensitivity of 105 of 140 (75%) for wrist/hand and finger examinations in one hospital versus 125 of 138 (91%) and 150 of 160 (94%) ($p = .004$) at the two others, but no differences in overall sensitivity or specificity were observed across all hospitals.

Lastly, use of the AI tool improved overall reader sensitivity (11 percentage points; $p < .001$) while maintaining specificity (0.6 percentage points; $p = .34$), the researchers reported.

“No differences in AI performance were observed across centers, and AI assistance was associated with higher reader sensitivity,” the authors wrote.

Next steps will be to evaluate the device’s performance before and after local calibration and to develop frameworks for continuous performance monitoring, the authors wrote. Prospective validation of workflow efficiency and patient outcomes in emergency settings will also be needed to support broader clinical implementation, the group concluded.

CLINICAL NEWS | MRI

Can MRI replace the PSA test in prostate cancer screening?

Kate Madden Yee

Jun 3, 2024

MRI isn't yet ready to replace prostate-specific antigen (PSA) testing as a first-line screening exam for prostate cancer, researchers have reported.

A team led by Roman Gulati of Fred Hutchinson Cancer Center in Seattle found that "despite the potential attractiveness of first-line imaging-based [prostate cancer] screening, [a] microsimulation model showed that first-line [biparametric MRI]-based screening substantially increased rates of false-positive test results, prostate biopsy, and overdiagnosis without proportionately substantial reductions in prostate cancer mortality compared with first-line PSA testing with reflex [multiparametric MRI]." The study findings were published June 3 in *Annals of Internal Medicine*.

First-line prostate cancer screening is currently performed with PSA testing, and in men with elevated PSA levels, may be followed by multiparametric MRI (mpMRI). In recent years, first-line biparametric MRI (bpMRI) screening has been proposed as an alternative to mpMRI; bpMRI uses T2-weighted images with diffusion-weighted imaging [DWI], while mpMRI adds dynamic contrast-enhanced [DCE] imaging -- with or without spectroscopy, the authors explained.
The draw of using MRI to diagnose prostate cancer is that it could streamline patient care, according to an editorial that accompanied the study.

"Replacing PSA testing with MRI would reduce the need for multiple consultations, thereby possibly improving efficiency and patient satisfaction," wrote a team led by Daniel Joyce, MD, of Vanderbilt University Medical Center in Nashville, TN. "Biparametric MRI (bpMRI), which omits the contrast-enhanced phases and thereby decreases cost and study duration, has been shown to be equivalent to multiparametric MRI in cancer detection and may further increase the value of MRI use in prostate cancer screening."

Gulati and colleagues compared both clinical effectiveness and cost-effectiveness of bpMRI versus PSA-based for prostate cancer screening via a microsimulation model based on data from the Surveillance, Epidemiology, and End Results (SEER) database and randomized trials, culling information for 1,000 men aged 55 years with no prior prostate cancer screening or diagnosis.

The proposed intervention was biennial screening from 55 to 69 years using first-line PSA testing (test-positive threshold: 4 mg/L) -- with or without second-line mpMRI -- or first-line bpMRI (test-positive threshold: Prostate Imaging Reporting and Data System [PI-RADS] 3 to 5 or 4 to 5), followed by biopsy-guided MRI or MRI plus transrectal ultrasonography. The investigators tracked the types of screening tests, any biopsies, diagnoses, overdiagnoses, treatments, prostate cancer deaths, quality-adjusted and unadjusted life-years saved, and costs.

Gulati's group found the following:

Comparison of first-line PSA testing to first-line bpMRI for prostate cancer screening in 1,000 men

Measure	First-line PSA testing	First-line bpMRI
Deaths prevented	3	2
Additional life years	30	10
Number of biopsies	1,506	4,174
Number of overdiagnoses	38	124

It also found that using conventional cost-effectiveness thresholds, first-line PSA testing with mpMRI followed by either biopsy approach for men with PI-RADS 4 to 5 results demonstrated the greatest net monetary benefits.

"First-line PSA testing remained more cost-effective even if bpMRI was free, all men with low-risk [prostate cancer] underwent surveillance, or screening was quadrennial," the group wrote.

The study underscores a need for more research, Joyce and colleagues noted in their editorial.

"[This] cost-effectiveness analysis of a bpMRI-first prostate cancer screening approach highlights the need for a more robust understanding of the true comparative diagnostic accuracy of bpMRI compared with PSA testing followed by standard template biopsy, the financial toxicity associated with modern prostate cancer screening practices, and how to select the best patients for prostate biopsy through incorporation of biomarkers, imaging, and patient risk factors," they wrote. "While we await such evidence, rigorous cost-effectiveness analyses can and should be considered in guideline recommendations to encourage physicians to pursue the highest-value management strategy for their patients."