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Letters to the Editor

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Molecular Breast Imaging Deserves Fair and Balanced Consideration

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I read with interest the recent "From the Editor" written by Dr Harvey (1) discussing the recent article from Dr Hendrick titled "Radiation Doses and Risks in Breast Screening" (2). While I agree with many statements from Dr Harvey and Dr Hendrick, the results of Dr Hendrick's article may mislead readers, given the one-sided presentation of the risks of each screening modality without discussing the corresponding benefits. Indeed, Walter Huda, PhD, wrote that "it is inappropriate to only compute the total number of cancers in a patient population that undergoes radiologic examinations because these computations ignore the likely enormous collective benefits associated with indicated examinations" (3).

I fear that Dr Hendrick's results will limit access to molecular breast imaging (MBI) for supplemental screening. I was similarly troubled that Dr Harvey wrote that the "total body dose" of MBI "limits utility." Most nuclear medicine studies require systemic radiation, yet these are routinely performed given the high net benefit of each exam. The net benefit of MBI for supplemental screening is five to nine times higher than the risk based on prior estimates by Dr Hendrick and myself with Dr Brown (4,5). Surprising to some, MBI could be the safest option for supplemental screening that currently exists given the potential for severe iodinated contrast reactions with contrast-enhanced mammography, the unknown consequences of gadolinium deposition from contrast-enhanced breast MRI, and the precariously low incremental cancer detection rates of both tomosynthesis and ultrasound.

Unfortunately, MBI has received infrequent support from the breast imaging community. Breast imaging radiologists need to leave all biases behind and objectively evaluate the MBI literature for net benefit instead of only risk. Breast radiologists should also support every supplemental screening modality with promise, including MBI.

Finally, Dr Harvey states, "Will I wonder at some point, 'How did we ever think we were finding enough cancers on mammography alone?'" (1). I propose that there is no need to wonder—we already know that mammography does not detect enough cancers in women with dense breast tissue, and this is a real, substantial, nontheoretical risk. For this reason, above all, let's give MBI a fair chance.

Conflict of Interest Statement

Dr Covington is a consultant for Hologic, Inc., for educational speaking on contrast-enhanced mammography.

References

1. Harvey JA. Screening: looking into the crystal ball. *J Breast Imag* 2020;2(3):177–178.
2. Hendrick RE. Radiation doses and risks in breast screening. *J Breast Imag* 2020;2(3):188–200.
3. Huda W. Radiation risks: what is to be done? *AJR Am J Roentgenol* 2015;204(1):124–127.
4. Hendrick RE, Tredennick T. Benefit to radiation risk of breast-specific gamma imaging compared with mammography in screening asymptomatic women with dense breasts. *Radiology* 2016;281(2):583–588.
5. Brown M, Covington MF. Comparative benefit-to-radiation risk ratio of molecular breast imaging, two-dimensional full-field digital mammography with and without tomosynthesis, and synthetic mammography with tomosynthesis. *Radiology* 2019;1(1).

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Comment on "Radiation Doses and Risks in Breast Screening"

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The recent article by Dr Hendrick (1) paints a bleak picture of molecular imaging techniques in terms of the estimated risk of radiation-caused cancer incidence (RCCI). While it is a theoretical exercise in risk assessment, it is likely to be widely quoted as the basis for recommending or rejecting

a particular screening modality, with a profound effect on physician's choices of screening modalities.

Rather than debate the nuances of the methodology (2), we felt the reader may better appreciate the magnitude of the risk estimates when put in the context of natural background radiation.

Using the Environmental Protection Agency radiation dose calculator (3), we calculated the annual natural background radiation dose for residents of Colorado and Louisiana at 9.3 mSv/year and 1.7 mSv/year, respectively. The cumulative radiation doses for women age 30 are 279 mSv and 51 mSv, respectively. Using the Biological Effects of Ionizing Radiation (BEIR) VII methodology, the estimated RCCIs are 6498 cases and 1188 cases, respectively. These cancer estimates are 1 to 2 orders of magnitude greater than those presented in table 5 (1). Even 12 months of living in Colorado carries with it an RCCI of ~100 cases. If the methodology utilized by Dr Hendrick is truly applicable at low doses, it should warrant warnings to the public of the risks associated with living in states with high natural background radiation. More importantly, it should make discussion of the relative risks of the screening modalities moot, and we should recognize that the risks from the various screening modalities, if any, are trivial relative to those from natural sources and focus on the modality that offers the highest cancer detection rate.

Interestingly, the actual annual cancer incidences in Colorado and Louisiana are 391.8/100000 and 432.1/100 000, respectively (4). The absence of any RCCIs in Colorado relative to Louisiana either indicates a failure of the BEIR VII methodology or reflects the fact that radiation-induced cancers represent a negligible percentage of all cancers. We—and many academic societies (5)—call for an end to the use of this flawed theoretical model to "calculate" spurious biologic risk, which in turn thwarts the adoption of imaging techniques demonstrated to improve the detection of breast cancer.

Conflict of Interest Statement

C.B. Hruska and M.K. O'Connor receive royalties for licensed technologies, as per the agreement between Mayo Clinic and a manufacturer of molecular breast imaging systems. No other authors have any conflicts to disclose.

References

1. Hendrick RE. Radiation doses and risks in breast screening. *J Breast Imag* 2020;2(3):188–200.
2. National Research Council of the National Academies. *Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII, Phase 2—Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation*. Washington, DC: National Academies Press; 2006.
3. Environmental Protection Agency. Radiation dose calculator. Available at: https://www.epa.gov/radiation/calculate-your-radiation-dose. Accessed August 18, 2020.
4. Centers for Disease Control and Prevention. United States cancer statistics: data visualizations. 2017. Available at: https://gis.cdc.gov/Cancer/USCS/DataViz.html. Accessed August 18, 2020.
5. American Association of Physicists in Medicine. Position statement of the American Association of Physicists in Medicine. Radiation risks from medical imaging procedures. 2011, affirmed November 2012. Available at: http://www.aapm.org/org/policies/details.asp?id=318&type=PP. Accessed August 18, 2020.

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Response to Two Letters Concerning Radiation Doses and Risks in Breast Screening

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I thank both authors for their letters concerning my recent "Science of Screening" article on radiation doses and risks (1). I was invited to write this article and based it on the best available evidence on radiation risks. The National Academy of Sciences' Biological Effects of Ionizing Radiation (BEIR) VII radiation risk estimates are the most relevant to breast imaging because they are age specific and gender specific, and they are the most credible. BEIR VII assumes a linear, no-threshold estimate of risk versus dose at low doses based on the linear dose–risk relationship that exists at organ doses higher than 100 mGy (2). Such an assumption is needed because reliable studies at low-dose exposures do not exist and would require millions of exposed subjects to have adequate power. Since radiologists and medical physicists have a duty to protect patients from unnecessary radiation, it would be irresponsible to assume otherwise about the extrapolation of risk versus dose to low-dose levels.

With regard to the higher radiation doses and risks by geographic location, there are greater cancer risks due to natural background radiation in Colorado than in Louisiana (3). It would be unwise, however, to attempt to correlate those higher risks of cancer induction by location without controlling for other risk factors such as smoking, diet, obesity, and chemical exposure. Louisiana residents in particular suffer high levels of manufacturing chemical exposure compared to Colorado residents (4). Radiologists and other physicians do not usually recommend where people should live, but they are often asked to recommend breast cancer screening tests, and that is why understanding the radiation risks and potential benefits of those tests is important.

One letter decries my article's use of "flawed theoretical models" to "'calculate' spurious biological risks." The other cites Dr Huda's warning about computing the total number of cancers in a patient population without noting the collective benefits associated with the exam. My response is that it is impossible to compare risks and benefits of various

breast screening tests, as my article and others referenced therein do, without first estimating the risks in terms of cancers induced and deaths caused by ionizing radiation.

Both letters expressed concerns that my article casts molecular breast imaging (MBI) in a dim light as a screening tool. That was (and is) not my intent. I would note that the clinical data supporting MBI as a supplemental screening tool, and the benefit to risk ratios that result, apply only to women with dense breasts who receive a low-dose MBI exam consisting of a 300 MBq (8 mCi) drawn dose of Technetium-99m sestamibi (5,6).

Conflict of Interest Statement

Dr Hendrick has served as a consultant to GE Healthcare on work unrelated to his referenced papers or this letter.

References

1. Hendrick RE. Radiation doses and risks in breast screening. *J Breast Imag* 2020;2(3):188–200.
2. National Research Council of the National Academies. *Health Risks From Exposure to Low Levels of Ionizing Radiation: BEIR VII, Phase 2—Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation*. Washington, DC: National Academies Press; 2006.
3. Institute for Science and International Security. Table 7: background radiation in Denver: average annual dose equivalent of ionizing radiation and risk. Available at: https://isis-online.org/risk/tab7. Accessed August 14, 2020.
4. Baurick T. Welcome to "Cancer Alley," where toxic air is about to get worse. The Times-Picayune and The Advocate, Oct. 30, 2019. Available at: https://www.propublica.org/article/welcome-to-cancer-alley-where-toxic-air-is-about-to-get-worse. Accessed August 14, 2020.
5. Rhodes DJ, Hruska CB, Conners AL, et al. Journal club: molecular breast imaging at reduced radiation dose for supplemental screening in mammographically dense breasts. *AJR Am J Roentgenol* 2015;204(2):241–251.
6. Hendrick RE, Tredennick T. Benefit to radiation risk of breast-specific gamma imaging compared with mammography in screening asymptomatic women with dense breasts. *Radiology* 2016;281(2):583–588.

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Comment on "Role of Breast Imaging Radiologists as Advocates for Screening Mammography"

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We read with great interest the article "Role of Breast Imaging Radiologists as Advocates for Screening Mammography," published April 10, 2020 (1). We commend the authors on their comprehensive overview of the myriad of advocacy opportunities for breast radiologists with regards to screening mammography. It is with respect that we would like to offer additional efficacious opportunities for advocacy in the community, because supporting local and national legislation and other forms of public service is an important part of the radiologist's role.

For example, the state of Colorado has passed multiple pieces of legislation in recent years regarding increasing access to, the education of, and the awareness of breast health. These include Senate Bill 17–142 Breast Density Notification Required (signed into law in 2017) and House Bill 19–1301 Health Insurance For Breast Imaging (signed into law in 2019) (2).

Surveys have demonstrated that patients who knew or wanted to know their breast density had stronger intentions or a higher likelihood of getting screening mammograms (3,4). Additionally, women who have insurance coverage are more likely to report having had a screening mammogram in the past two years compared with uninsured women (5).

Breast imaging radiologists can participate in stakeholder meetings, write and edit legislation, and testify on bills in writing or in person. These opportunities are reinforced when radiologists play active roles in advocacy or government relations committees, legislative councils, and health policy-making sessions of their state and/or national specialty and medical societies. We also encourage breast imaging radiologists to seek out and serve on regional and national advisory boards. For example, the state of Colorado's Department of Public Health & Environment has a breast and cervical cancer screening advisory board. This board is composed of diverse community volunteers, and breast imaging radiologists have held seats on this board in the recent past.

Thank you for considering our additions to the roles and contributions of breast imaging radiologists in advocacy for screening mammography.

Conflict of Interest Statement

None declared.

References

1. Omofoye TS, Parikh JR. Role of breast imaging radiologists as advocates for screening mammography. *J Breast Imag* 2020;2(3):259–263.
2. Colorado General Assembly. Bills, resolutions, & memorials. Available at: https://leg.colorado.gov/bills. Accessed July 13, 2020.
3. Santiago-Rivas M, Benjamin S, Andrews JZ, Jandorf L. Breast density awareness and knowledge, and intentions for breast cancer screening in a diverse sample of women age eligible for mammography. *J Cancer Educ* 2019;34(1):90–97.
4. Yeh VM, Schnur JB, Margolies L, Montgomery GH. Dense breast tissue notification: impact on women's perceived risk, anxiety, and intentions for future breast cancer screening. *J Am Coll Radiol* 2015;12(3):261–266.

5. Kaiser Family Foundation. Coverage of breast cancer screening and prevention services fact sheet. Available at: https://www.kff.org/womens-health-policy/fact-sheet/coverage-of-breast-cancer-screening-and-prevention-services/. Accessed July 13, 2020.

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Reply to Comment on "Role of Breast Imaging Radiologists as Advocates for Screening Mammography"

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We sincerely thank Drs Kattapuram and Hoagland for their thoughtful letter of response (1) to our article (2). The purpose of our article was to provide the rationale for breast radiologists to become involved in local advocacy for screening and to offer a myriad of approaches to support this important role. Our manuscript was tailored toward providing our audience of breast radiologists with an overview applicable to daily clinical practice.

We heartily support the spirit of the letter provided by Drs Kattapuram and Hoagland. The letter further delves into specifics and examples regarding the critical roles of political advocacy and public service and how they impact all breast radiologists. We embrace the inclusion of more radiologists in these types of advocacy efforts (and the highlighting of more opportunities for such), which are often at a regional or national level, to promote breast screening because of its significant potential impact in reducing breast cancer morbidity and mortality.

Conflict of Interest Statement

None declared.

References

1. Kattapuram T, Hoagland L. Comment on "Role of Breast Imaging Radiologists as Advocates for Screening Mammography." *J Breast Imag* 2020;2(6):521.
2. Omofoye TS, Parikh JR. Role of breast imaging radiologists as advocates for screening mammography. *J Breast Imag* 2020;2(3):259–263.

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Comment on "Rare Cancer on the Rise: An Educational Review of Breast Implant-associated Anaplastic Large Cell Lymphoma"

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We read with interest the article "Rare Cancer on the Rise: An Educational Review of Breast Implant-associated Anaplastic Large Cell Lymphoma," published on June 26, 2020 (1). We want to congratulate the authors for an excellent review regarding the diagnosis, imaging findings, and management of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL).

Since 2017, we have started a study protocol to evaluate breast implants and their complications. And we agree with the authors that knowledge about BIA-ALCL etiology remains poorly understood, as there is a large variance in incidence in such cases. However, our group believes that through this letter, we can contribute two important points:

1. In the context of BIA-ALCL lymphomagenesis, we believe that an important factor in its complex process is "gel bleed"—the leakage of silicone particles from an intact implant secondary to the fragility of the elastomer. These silicone particles, when in contact with a capsule, cause an immune-mediated response that could certainly contribute to the development of BIA-ALCL (2).
2. As described in the article, "approximately 9%–13% of delayed seromas are found to be due to BIA-ALCL" (1). Therefore, we can assume that most cases developed a seroma related to another pathology; considering this, we have proposed the silicone-induced granuloma of the breast implant capsule (SIGBIC) as a differential diagnosis to BIA-ALCL (3).

The SIGBIC consists of silicone-induced granuloma formation in the breast implant fibrous capsule without signs of implant rupture and without malignant cells on histology. We described the three breast MRI findings as (1) a black-drop sign, (2) a mass with hyperintense signal on T2, and (3) late contrast enhancement (2–5).

The clinical–radiological presentation of lymphoma and granuloma induced by silicone has shown to be increasingly similar, while the incidence of lymphoma is still much lower than the prevalence of findings suggestive of it.

In summary, compared to reports in the literature, it is becoming increasingly evident that granuloma and lymphoma are possibly spectra of the same disease with a common trigger—gel bleed—and the difference between BIA-ALCL and SIGBIC is probably the exacerbated or uncontrolled immune response.

Conflict of Interest Statement

None declared.

References

1. Mitry MA, Sogani J, Sutton EJ, et al. Rare cancer on the rise: an educational review of breast implant-associated anaplastic large cell lymphoma. *J Breast Imag* 2020;2(4):398–407.
2. Fleury EdFC. Silicone induced granuloma of breast implant capsule (SIGBIC) diagnosis: breast magnetic resonance (BMR) sensitivity to detect silicone bleeding. *PLoS ONE* 2020;15(6):e0235050.
3. Castro C, Fernandes D, Mendonça M, Roveda Junior D, Badan G, Fleury EdFC. Silicone-induced granuloma of breast implant capsule mimicking anaplastic large cell lymphoma. *Breast J* 2020;26(5):1028–1030.
4. Castro C, Campos MSDdA, Roveda Jr D, Fleury EdFC. Synchronous silicone-induced granuloma (SIG) of breast implant capsule (BIC) and gluteal implant capsule (GIC): what to learn [published online ahead of print May 29, 2020]. *Breast J* 2020. doi:10.1111/tbj.13901.
5. Fleury EdFC, Rêgo MM, Ramalho LC, et al. Silicone-induced granuloma of breast implant capsule (SIGBIC): similarities and differences with anaplastic large cell lymphoma (ALCL) and their differential diagnosis. *Breast Cancer (Dove Med Press)* 2017;9:133–140.

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Comment on "Unknown Challenge #8: Pneumomastia": Additional Differential Diagnosis to Pneumomastia

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I reviewed with great interest "Unknown Challenge #8: Pneumomastia," published on June 15, 2020 (1). An additional and potentially dangerous differential diagnosis that can be considered in patients presenting with air tracking along the breast tissue is ozone therapy. The Food and Drug Administration has stated that ozone is a "toxic gas with no known useful medical applications" (2). Consequently, this type of therapy is generally not used in the United States. Medical doctors have long considered ozone dangerous, as the O_3 molecule is unstable; however, naturopaths continue to study and utilize ozone for a variety of ailments, including infections, musculoskeletal complaints, cardiovascular disease, and cancer therapy (3). At our comprehensive breast imaging center, we see patients undergoing naturopathic alternative therapies in addition to, or instead of, conventional medical therapies (Figure 1). Please consider this additional differential diagnosis and its potential associated dangers.

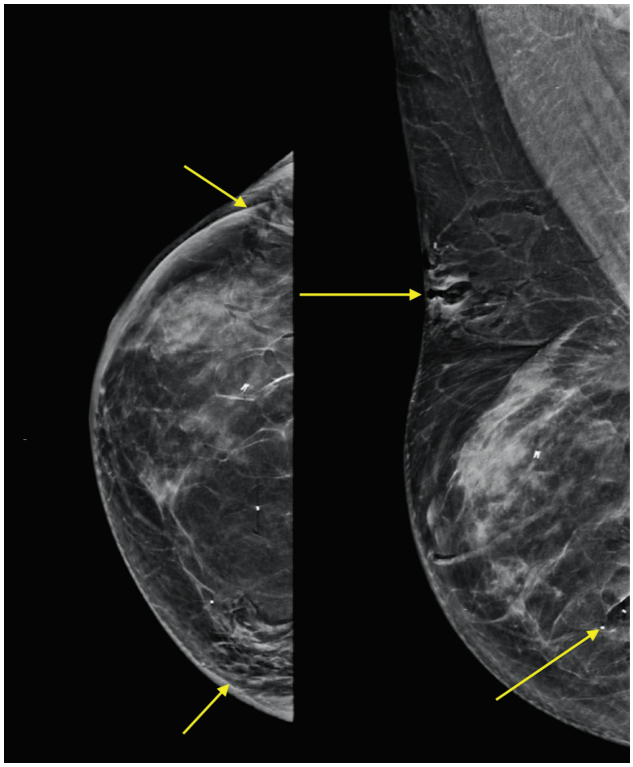

Figure 1. Synthetic craniocaudal and mediolateral oblique views of a 56-year-old patient with a personal history of a 6-cm high-grade ER+PR+HER2+ invasive ductal breast cancer treated with lumpectomy, radiation, and adjuvant therapy. At the time of routine follow-up imaging several years after the initial diagnosis, the patient had traveled to Mexico and self-reported therapy with direct ozone injections to the right breast. Arrows show scattered areas of lucency consistent with pneumomastia. As the patient presented for routine screening, there was no opportunity to educate the patient regarding the potential dangers of ozone therapy.

Conflict of Interest Statement

H.O.F. discloses consultant work for IBM Watson and ViewPoint Medical for work unrelated to this manuscript.

References

1. Entezari P, Scheel JR. Unknown case #8: 61-year-old woman presents for a screening mammogram. *J Breast Imag* 2020;2(4):408–409.
2. U.S. Food & Drug Administration. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=801.415. Accessed August 16, 2020.
3. Smith NL, Wilson AL, Gandhi J, Vatsia S, Khan SA. Ozone therapy: an overview of pharmacodynamics, current research, and clinical utility. *Med Gas Res* 2017;7(3):212–219.

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