# American College of Radiology ACR Appropriateness Criteria® Transgender Breast Cancer Screening

<u>Variant 1:</u>
Breast cancer screening. Transfeminine (male-to-female) patient, 40 years of age or older with past or current hormone use equal to or greater than 5 years. Average-risk patient.

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	May Be Appropriate	<b>∵</b>
Mammography screening	May Be Appropriate	<b>⊕⊕</b>
US breast	Usually Not Appropriate	0
MRI breast without and with IV contrast	Usually Not Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0

#### Variant 2:

Breast cancer screening. Transfeminine (male-to-female) patient, 25 to 30 years of age or older with past or current hormone use equal to or greater than 5 years. Higher-than-average risk (patient with personal history of breast cancer or chest irradiation at 10 to 30 years of age, patient with genetic predisposition to breast cancer, patient with family history of breast or ovarian cancer, and untested patient with first-degree relative with genetic predisposition to breast cancer).

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	<b>⊕⊕</b>
Mammography screening	Usually Appropriate	<b>⊕⊕</b>
US breast	Usually Not Appropriate	0
MRI breast without and with IV contrast	Usually Not Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0

# <u>Variant 3:</u> Breast cancer screening. Transfeminine (male-to-female) patient with no hormone use (or hormone use less than 5 years) at any age. Average-risk patient.

Procedure	Appropriateness Category	Relative Radiation Level
US breast	Usually Not Appropriate	0
Digital breast tomosynthesis screening	Usually Not Appropriate	<b>⊕⊕</b>
Mammography screening	Usually Not Appropriate	<b>⊕⊕</b>
MRI breast without and with IV contrast	Usually Not Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0

# Variant 4:

Breast cancer screening. Transfeminine (male-to-female) patient, 25 to 30 years of age or older with no hormone use (or hormone use less than 5 years). Higher-than-average risk (patient with personal history of breast cancer or chest irradiation at 10 to 30 years of age, patient with genetic predisposition to breast cancer, patient with family history of breast or ovarian cancer, and untested patient with first-degree relative with genetic predisposition to breast cancer).

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	May Be Appropriate	��
Mammography screening	May Be Appropriate	��
MRI breast without and with IV contrast	Usually Not Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0
US breast	Usually Not Appropriate	0

# <u>Variant 5:</u> Breast cancer screening. Transmasculine (female-to-male) patient with bilateral mastectomies ("top surgery") at any age and any risk.

Procedure	Appropriateness Category	Relative Radiation Level
US breast	Usually Not Appropriate	0
Digital breast tomosynthesis screening	Usually Not Appropriate	<b>∵</b>
Mammography screening	Usually Not Appropriate	��
MRI breast without and with IV contrast	Usually Not Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0

### Variant 6:

Breast cancer screening. Transmasculine (female-to-male) patient with reduction mammoplasty or no chest surgery, 40 years of age or older. Average-risk patient (less than 15% lifetime risk of breast cancer).

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	<b>∵</b>
Mammography screening	Usually Appropriate	€€
US breast	Usually Not Appropriate	0
MRI breast without and with IV contrast	Usually Not Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0

# Variant 7:

Breast cancer screening. Transmasculine (female-to-male) patient with reduction mammoplasty or no chest surgery, 30 years of age or older. Intermediate risk (patient with personal history of breast cancer, lobular neoplasia, atypical ductal hyperplasia, or 15% to 20% lifetime risk of breast cancer).

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	<b>∵</b>
Mammography screening	Usually Appropriate	<b>⊕⊕</b>
US breast	May Be Appropriate	0
MRI breast without and with IV contrast	May Be Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0

#### Variant 8:

Breast cancer screening. Transmasculine (female-to-male) patient with reduction mammoplasty or no chest surgery, 25 to 30 years of age or older. High risk (patient with genetic predisposition to breast cancer or untested patient with a first-degree relative with genetic predisposition to breast cancer, patient with a history of chest irradiation between 10 to 30 years of age, patient with 20% or greater lifetime risk of breast cancer).

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	<b>⊕⊕</b>
Mammography screening	Usually Appropriate	<b>∵</b>
MRI breast without and with IV contrast	Usually Appropriate	0
US breast	May Be Appropriate	0
MRI breast without IV contrast	Usually Not Appropriate	0

#### TRANSGENDER BREAST CANCER SCREENING

Expert Panel on Breast Imaging: Ann Brown, MD<sup>a</sup>; Ana P. Lourenco, MD<sup>b</sup>; Bethany L. Niell, MD, PhD<sup>c</sup>; Beth Cronin, MD<sup>d</sup>; Elizabeth H. Dibble, MD<sup>e</sup>; Maggie L. DiNome, MD<sup>f</sup>; Mita Sanghavi. Goel, MD, MPH<sup>g</sup>; Juliana Hansen, MD<sup>h</sup>; Samantha L. Heller, MD, PhD<sup>i</sup>; Maxine S. Jochelson, MD<sup>j</sup>; Baer Karrington<sup>k</sup>; Katherine A. Klein, MD<sup>l</sup>; Tejas S. Mehta, MD, MPH<sup>m</sup>; Mary S. Newell, MD<sup>n</sup>; Loren Schechter, MD<sup>o</sup>; Ashley R. Stuckey, MD<sup>p</sup>; Mary E. Swain, MD<sup>q</sup>; Jennifer Tseng, MD<sup>r</sup>; Daymen S. Tuscano, MD<sup>s</sup>; Linda Moy, MD<sup>t</sup>.

#### **Summary of Literature Review**

# Introduction/Background

Transgender is an umbrella term for any individual whose gender identity, or internal sense of self related to gender, differs from the sex assigned at birth. A nonbinary individual may have been assigned female or male at birth but does not strictly identify with either sex. A transfeminine person identifies with the female side of the gender spectrum but was assigned male at birth. These individuals may include transgender women, historically referred to as male-to-female transsexuals. A transmasculine person identifies with the male side of the gender spectrum but was assigned female at birth. These individuals may include transgender men, historically referred to as female-to-male transsexuals. For transgender and gender-nonconforming individuals, breast cancer screening recommendations are based on the sex assigned at birth, risk factors, and use of exogenous hormones.

A detailed discussion of the continuously evolving terminology in the context of caring for a great diversity of transgender people is beyond the scope of this document. As of the writing of this document, the terminology is derived from the University of California San Francisco (UCSF) Center of Excellence for Transgender Health (https://transcare.ucsf.edu/guidelines/terminology).

The incidence of breast cancer in the transgender community is largely unknown because of inadequate epidemiological information and a lack of longitudinal studies. Current evidence consists primarily of case reports and several cohort studies, all of which are retrospective. However, a younger age at the time of breast cancer diagnosis has been reported in transgender people [1-5].

Gender-affirming therapy can influence an individual's risk of developing certain cancers, including breast cancer [5,6]. Transgender patients may undergo either gender-affirming hormone treatment (previously known as cross-sex hormone treatment), surgical treatment, or a combination thereof as part of their transition. Updated clinical practice guidelines from the Endocrine Society allow earlier medical intervention for transgender youth beginning with pubertal hormone suppression once children first exhibit changes of puberty (Tanner stage 2) [7]. Hormone therapy plays an important role in developing secondary sex characteristics and is typically used for life. Transfeminine patients are usually treated with antiandrogens and estrogens, whereas transmasculine patients are treated with testosterone. Gender-affirming breast surgeries can include reduction mammoplasty or mastectomy—known as "top surgery"—in transgender men and breast augmentation with implants, autologous fat grafting, or both in transgender women. Although not a sanctioned practice, some individuals have had free injections of liquid substances, including silicone, into the breast for the purposes of augmentation [8].

The same breast pathology that occurs in cisgender women can be found in transgender women treated with gender-affirming hormone therapy. Mammary development includes the formation of ducts, lobules, and acini, which is histologically identical to cisgender females and should not be referred to as gynecomastia [4,9,10]. There are

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The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through representation of such organizations on expert panels. Participation on the expert panel does not necessarily imply endorsement of the final document by individual contributors or their respective organization.

published reports of benign breast entities, such as fibroadenomas, cysts, and lipomas [3,11], as well as breast malignancies that include ductal and lobular carcinomas and malignant phyllodes tumor [3,12].

Transgender patients can present with the same breast symptoms as cisgender patients, including palpable breast masses and breast pain as well as physiologic or pathologic nipple discharge. In particular, transgender women can experience nipple discharge related to hormone-induced hyperprolactinemia [13]. Please see the ACR Appropriateness Criteria® topics on "Palpable Breast Masses" [14], "Breast Pain" [15], and "Evaluation of Nipple Discharge" [16] for evaluation of these breast symptoms. Similarly, transgender patients may present with implant-related symptoms or complications. Please see the ACR Appropriateness Criteria® topic on "Breast Implant Evaluation" [17] or these symptoms.

# **Discussion of Procedures by Variant**

# Variant 1: Breast cancer screening. Transfeminine (male-to-female) patient, 40 years of age or older with past or current hormone use equal to or greater than 5 years. Average-risk patient.

Recommendations for breast cancer screening in transfeminine patients are typically based on the male sex assigned at birth, the number of years of feminizing hormone exposure, breast development, and any significant risk factors for breast cancer.

# **Digital Breast Tomosynthesis Screening**

There is no relevant data on the use of digital breast tomosynthesis (DBT) for breast cancer screening of transgender individuals in this clinical setting. Furthermore, no longitudinal data exist on screening transgender women for breast cancer with imaging. However, limited data on transgender individuals along with extrapolated data from cisgender studies suggest that digital mammography or DBT may be helpful to screen for breast cancer in transgender women. A Dutch cohort study of 3,489 transgender patients showed an increased risk of breast cancer in transgender women receiving gender-affirming hormone therapy compared with cisgender men (standardized incidence ratio [SIR]: 46.7, 95% confidence interval [CI]: 27.2-75.4) but not compared with eigender women (SIR: 0.3, 95% CI: 0.2–0.4) [2]. The risk of breast cancer increased over a relatively short hormone duration (median 18 years, range 7–37 years). Three previous studies concluded that the risk of breast cancer in transgender women is comparable with that of cisgender men [1,3,18]; however, the incidence was increased in transgender women who received hormone treatment (31.4 per 100,000 person-years compared with 1.2 per 100,000 person-years for cisgender men and 170 per 100,000 person-years for cisgender women) [1]. Any conclusions drawn from the existing literature are significantly limited by inconsistent dose and length of exposure to hormones as well as small sample size and relatively short duration of follow-up. Large prospective cisgender studies have shown that exogenous hormones, in particular estrogen and progestin, increase breast cancer risk in cisgender postmenopausal females [18-20], which could support a role for screening in this clinical setting. Additionally, in cisgender males, high estrogen levels associated with certain conditions, such as Klinefelter syndrome, liver disease, testicular dysfunction, and obesity, are recognized risk factors for developing breast cancer [21].

In the absence of definitive data on the risk of breast cancer in this clinical setting, some transgender health experts and professional societies have established guidelines recommending screening mammography in transgender women with ≥5 years of hormone use. However, the current recommendations range from annual or biennial mammograms starting at age 50 from the UCSF and Fenway Health to screening transgender women with the same frequency as cisgender women beginning at age 40 from the Endocrine Society [10].

In addition to planar images, DBT allows for creation and viewing of thin-section reconstructed images that decrease the lesion-masking effect of overlapping normal tissue, thereby decreasing false-positive recalls as well as improving cancer detection rates (CDRs) in breast cancer screening.

#### **Mammography Screening**

There are no relevant data on the use of digital mammography for breast cancer screening of transgender individuals in this clinical setting. Furthermore, no longitudinal data exist on screening transgender women for breast cancer with imaging. However, limited data on transgender individuals, along with extrapolated data from cisgender studies, suggest that digital mammography or DBT is helpful to screen for breast cancer in transgender women. A Dutch cohort study of 3,489 transgender patients showed an increased risk of breast cancer in transgender women receiving gender-affirming hormone therapy compared with cisgender men (SIR: 46.7, 95% CI: 27.2–75.4) but not compared with cisgender women (SIR: 0.3, 95% CI: 0.2–0.4) [2]. The risk of breast cancer increased over a relatively short hormone duration (median 18 years, range 7–37 years). Two previous studies concluded that the risk of breast cancer in transgender women is comparable with that in cisgender men [1,3]; however, the incidence

was increased in transgender women who received hormone treatment (31.4 per 100,000 person-years compared with 1.2 per 100,000 person-years for cisgender men and 170 per 100,000 person-years for cisgender women) [1]. Any conclusions drawn from the existing literature are significantly limited by inconsistent dose and length of exposure to hormones as well as small sample size and relatively short duration of follow-up. Large prospective cisgender studies have shown that exogenous hormones, in particular estrogen and progestin, increase breast cancer risk in cisgender postmenopausal females [18-20], which could support a role for screening in this clinical setting. Additionally, in cisgender males, high estrogen levels associated with certain conditions, such as Klinefelter syndrome, liver disease, testicular dysfunction, and obesity, are recognized risk factors for developing breast cancer [21].

In the absence of definitive data on the risk of breast cancer in this clinical setting, some transgender health experts and professional societies have established guidelines recommending screening mammography in transgender women with  $\geq 5$  years of hormone use. However, the current recommendations range from annual or biennial mammograms starting at age 50 from the UCSF and Fenway Health to screening transgender women with the same frequency as that of cisgender women beginning at age 40 from the Endocrine Society [10].

### MRI Breast Without and With IV Contrast

There is insufficient evidence to support the use of MRI breast without and with intravenous (IV) contrast to screen for breast cancer in this clinical setting. However, MRI screening may have limited use in patients who have undergone direct injection of particles such as silicone, mineral oil, liquid paraffin, or petroleum jelly to augment the breasts because fibrosis and injection granulomas can obscure the breast tissue on mammography and ultrasound (US). Hence, contrast-enhanced breast MRI is the preferred modality for breast cancer detection in patients who have undergone breast augmentation with free-particle injections [4,10].

#### **MRI Breast Without IV Contrast**

There is no relevant literature to support the use of MRI breast without IV contrast for screening in this clinical setting. However, transgender women may have breast implants placed for augmentation. For evaluation of implants and for discussion of the evidence regarding screening for implant rupture, please see the ACR Appropriateness Criteria® topic on "Breast Implant Evaluation" [17].

#### **US Breast**

There is insufficient evidence to support screening with US breast in this clinical setting. A small study of screening whole-breast US in 50 transgender women found no cancers [11]. The majority of patients were on estrogen therapy (94%) and had no family history of breast cancer (88%). However, the lack of incremental cancer detection may be secondary to the small sample size.

Variant 2: Breast cancer screening. Transfeminine (male-to-female) patient, 25 to 30 years of age or older with past or current hormone use equal to or greater than 5 years. Higher-than-average risk (patient with personal history of breast cancer or chest irradiation at 10 to 30 years of age, patient with genetic predisposition to breast cancer, patient with family history of breast or ovarian cancer, and untested patient with first-degree relative with genetic predisposition to breast cancer).

Recommendations for breast cancer screening in transfeminine patients are typically based on the male sex assigned at birth, the number of years of feminizing hormone exposure, breast development, and any significant risk factors for breast cancer.

### **Digital Breast Tomosynthesis Screening**

There are no relevant data on the use of DBT for breast cancer screening of transgender individuals in this clinical setting. Furthermore, no longitudinal data on screening transgender women for breast cancer with imaging exist. However, limited data on transgender individuals, along with extrapolated data from cisgender studies, suggest that digital mammography or DBT is helpful to screen for breast cancer in higher-than-average-risk transgender women. A Dutch cohort study of 3,489 transgender patients showed an increased risk of breast cancer in transgender women receiving gender-affirming hormone therapy compared with cisgender men (SIR: 46.7, 95% CI: 27.2–75.4) but not compared with cisgender women (SIR 0.3: 95% CI: 0.2–0.4) [2]. The risk of breast cancer increased over a relatively short hormone duration (median 18 years, range 7–37 years). Three previous studies concluded that the risk of breast cancer in transgender women is comparable with that of cisgender men [1,3,18]; however, the incidence was increased in transgender women who received hormone treatment (31.4 per 100,000 person-years compared with 1.2 per 100,000 person-years for cisgender men and 170 per 100,000 person-years for cisgender women) [1]. Any conclusions drawn from the existing literature are significantly limited by inconsistent dose and length of exposure

to hormones as well as small sample size and relatively short duration of follow-up. Large prospective cisgender studies have shown that exogenous hormones, in particular estrogen and progestin, increase breast cancer risk in cisgender postmenopausal females [18-20], which could support a role for screening in this clinical setting.

Although the relative risk of breast cancer associated with exogenous hormone therapy in transfeminine patients remains to be clearly defined, data extrapolated from cisgender men support screening mammography in this clinical setting. One retrospective study of cisgender men at increased risk of breast cancer (ages 18–96 years; median: 55 years) showed a CDR of 18 per 1,000 screening mammograms, including a subset performed with DBT [22]. The use of DBT was limited to only 46 studies (2.2%). A smaller retrospective cohort study and 3 case reports also support screening higher-than-average-risk cisgender men for breast cancer [22-24]. Recognized risk factors for the development of breast cancer in cisgender men include personal history of breast cancer, genetic predisposition (ie, Breast Cancer gene [BRCA] mutations, Ashkenazi descent), previous radiation exposure, family history of breast or ovarian cancer, and elevated estrogen levels (ie, Klinefelter's syndrome, obesity, etc) [21-23]. Because of a paucity of data, a finer classification of breast cancer risk in this patient population is not currently possible.

In the absence of definitive data, some transgender health experts and professional societies recommend digital mammography or DBT to screen for breast cancer in transgender women with higher-than-average risk of breast cancer (<a href="https://transcare.ucsf.edu/guidelines/breast-cancer-women">https://transcare.ucsf.edu/guidelines/breast-cancer-women</a>). There is no consensus on the age at which to initiate screening in this clinical setting. The Endocrine Society recommends screening transgender women with the same frequency as cisgender women [10]. The ACR screening recommendation for high-risk cisgender women is annual screening mammography beginning 10 years earlier than an affected relative at the age of diagnosis (but not before age 30) or 8 years after radiation therapy (but not before age 25) [25].

In addition to planar images, DBT allows for creation and viewing of thin-section reconstructed images that decrease the lesion-masking effect of overlapping normal tissue, thereby decreasing false-positive recalls as well as improving CDR in breast cancer screening.

# **Mammography Screening**

There are no relevant data on the use of digital mammography for breast cancer screening of transgender individuals in this clinical setting. Furthermore, no longitudinal data on screening transgender women for breast cancer with imaging exist. However, limited data on transgender individuals, along with extrapolated data from cisgender studies, suggest that digital mammography or DBT is helpful to screen for breast cancer in higher-than-averagerisk transgender women. A Dutch cohort study of 3,489 transgender patients showed an increased risk of breast cancer in transgender women receiving gender-affirming hormone therapy compared with cisgender men (SIR: 46.7, 95% CI: 27.2–75.4) but not compared with cisgender women (SIR: 0.3, 95% CI: 0.2–0.4) [2]. The risk of breast cancer increased over a relatively short hormone duration (median 18 years, range 7-37 years). Three previous studies concluded that the risk of breast cancer in transgender women is comparable with that of cisgender men [1,3,18]; however, the incidence was increased in transgender women who received hormone treatment (31.4 per 100,000 person-years compared with 1.2 per 100,000 person-years for cisgender men and 170 per 100,000 person-years for cisgender women) [1]. Any conclusions drawn from the existing literature are significantly limited by inconsistent dose and length of exposure to hormones as well as small sample size and relatively short duration of follow-up. Large prospective cisgender studies have shown that exogenous hormones, in particular estrogen and progestin, increase breast cancer risk in cisgender postmenopausal females [18-20], which could support a role for screening in this clinical setting.

Although the relative risk of breast cancer associated with exogenous hormone therapy in transfeminine patients remains to be clearly defined, data extrapolated from cisgender men support screening mammography in this clinical setting. One retrospective study of cisgender men at increased risk of breast cancer (ages 18–96 years; median: 55 years) showed a CDR of 18 per 1,000 screening mammograms, including a subset performed with DBT [22]. The use of DBT was limited to only 46 studies (2.2%). A smaller retrospective cohort study and 3 case reports also support screening higher-than-average-risk cisgender men for breast cancer [22-24]. Recognized risk factors for the development of breast cancer in cisgender men include personal history of breast cancer, genetic predisposition (ie, BRCA mutations, Ashkenazi descent), previous radiation exposure, family history of breast or ovarian cancer, and elevated estrogen levels (ie, Klinefelter's syndrome, obesity, etc) [21-23]. Because of a paucity of data, a finer classification of breast cancer risk in this patient population is not currently possible.

In the absence of definitive data, some transgender health experts and professional societies recommend digital mammography or DBT to screen for breast cancer in transgender women with higher-than-average risk of breast cancer (<a href="https://transcare.ucsf.edu/guidelines/breast-cancer-women">https://transcare.ucsf.edu/guidelines/breast-cancer-women</a>). There is no consensus on the age at which to initiate screening in this clinical setting. The Endocrine Society recommends screening transgender women with the same frequency as cisgender women [10]. The ACR screening recommendation for high-risk cisgender women is annual screening mammography beginning 10 years earlier than an affected relative at the age of diagnosis (but not before age 30) or 8 years after radiation therapy (but not before age 25) [25].

## **MRI Breast Without and With IV Contrast**

There is insufficient evidence to support the use of MRI breast without and with IV contrast to screen for breast cancer in this clinical setting. However, MRI screening may have limited use in patients who have undergone direct injection of particles, such as silicone, mineral oil, liquid paraffin, or petroleum jelly, to augment the breasts because fibrosis and injection granulomas can obscure the breast tissue on mammography and US. Hence, contrast-enhanced breast MRI is the preferred modality for breast cancer detection in patients who have undergone breast augmentation with free-particle injections [4,10].

For evaluation of implants and for discussion of the evidence regarding screening for implant rupture, please see the ACR Appropriateness Criteria® topic on "Breast Implant Evaluation" [17].

### **MRI Breast Without IV Contrast**

There is no relevant literature to support the use of MRI breast without IV contrast for screening in this clinical setting. However, transgender women may have breast implants placed for augmentation. For evaluation of implants and for discussion of the evidence regarding screening for implant rupture, please see the ACR Appropriateness Criteria® topic on "Breast Implant Evaluation" [17].

#### **US Breast**

There is no relevant literature to support the use of US for breast cancer screening in this clinical setting.

# Variant 3: Breast cancer screening. Transfeminine (male-to-female) patient with no hormone use (or hormone use less than 5 years) at any age. Average-risk patient.

Recommendations for breast cancer screening in transfeminine patients are typically based on the male sex assigned at birth, the number of years of feminizing hormone exposure, breast development, and any significant risk factors for breast cancer.

#### **Digital Breast Tomosynthesis Screening**

There is no relevant literature to support the use of DBT for breast cancer screening in this clinical setting. In the absence of identifiable risk factors for breast cancer, general screening has no role because of an overall low prevalence of disease. The lifetime risk of breast cancer in transfeminine patients with no hormone use and no significant risk factors is considered to be equivalent to the average risk in cisgender men, which is 0.1% (compared with 12.4% in the average-risk cisgender female) [1,26].

# **Mammography Screening**

There is no relevant literature to support the use of DBT for breast cancer screening in this clinical setting. In the absence of identifiable risk factors for breast cancer, general screening has no role because of an overall low prevalence of disease. The lifetime risk of breast cancer in transfeminine patients with no hormone use and no significant risk factors is considered to be equivalent to the average risk in cisgender men, which is 0.1% (compared with 12.4% in the average-risk cisgender female) [1,26].

#### MRI Breast Without and With IV Contrast

There is no relevant literature to support the use of MRI breast without and with IV contrast to screen for breast cancer in this clinical setting.

#### **MRI Breast Without IV Contrast**

There is no relevant literature to support the use of MRI breast without IV contrast for screening in this clinical setting. However, transgender women may have breast implants placed for augmentation. For evaluation of implants and for discussion of the evidence regarding screening for implant rupture, please see the ACR Appropriateness Criteria<sup>®</sup> topic on "Breast Implant Evaluation" [17].

#### US Breast

There is no relevant literature to support the use of US for breast cancer screening in this clinical setting.

Variant 4: Breast cancer screening. Transfeminine (male-to-female) patient, 25 to 30 years of age or older with no hormone use (or hormone use less than 5 years). Higher-than-average risk (patient with personal history of breast cancer or chest irradiation at 10 to 30 years of age, patient with genetic predisposition to breast cancer, patient with family history of breast or ovarian cancer, and untested patient with first-degree relative with genetic predisposition to breast cancer).

Recommendations for breast cancer screening in transfeminine patients are typically based on the male sex assigned at birth, the number of years of feminizing hormone exposure, breast development, and any significant risk factors for breast cancer.

# **Digital Breast Tomosynthesis Screening**

There are no relevant data on the use of DBT for breast cancer screening of transgender individuals in this clinical setting. Furthermore, no longitudinal data on screening transgender women for breast cancer with imaging exist. However, limited data from risk-comparable cisgender men suggest that screening mammography or DBT may be beneficial in this clinical setting. A retrospective study of 1,869 cisgender men with higher-than-average risk (ages 18–96 years; median 55 years) reported a CDR of 18 per 1,000 examinations using digital mammography or DBT to screen for breast cancer [22]. The use of DBT was limited to only 46 studies (2.2%). A smaller retrospective cohort study and 3 case reports also support screening higher-than-average-risk cisgender men for breast cancer [22,23]. Recognized risk factors for the development of breast cancer in cisgender men include personal history of breast cancer, genetic predisposition (ie, BRCA mutations, Ashkenazi descent), previous radiation exposure, family history of breast or ovarian cancer, and elevated estrogen levels (ie, Klinefelter's syndrome, obesity, etc) [21-23]. Because of a paucity of data, a finer classification of breast cancer risk in this patient population is not currently possible.

In addition to planar images, DBT allows for creation and viewing of thin-section reconstructed images that decrease the lesion-masking effect of overlapping normal tissue, thereby decreasing false-positive recalls as well as improving CDR in breast cancer screening.

# **Mammography Screening**

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# MRI Breast Without and With IV Contrast

There is insufficient evidence to support the use of MRI breast without and with IV contrast to screen for breast cancer in this clinical setting. However, MRI screening may have limited use in patients who have undergone direct injection of particles, such as silicone, mineral oil, liquid paraffin, or petroleum jelly, to augment the breasts because fibrosis and injection granulomas can obscure the breast tissue on mammography and US. Hence, contrast-enhanced breast MRI is the preferred modality for breast cancer detection in patients who have undergone breast augmentation with free-particle injections [4,10].

For evaluation of implants and for discussion of the evidence regarding screening for implant rupture, please see the ACR Appropriateness Criteria<sup>®</sup> topic on "Breast Implant Evaluation" [17].

### **MRI Breast Without IV Contrast**

There is no relevant literature to support the use of MRI breast without IV contrast for screening in this clinical setting. However, transgender women may have breast implants placed for augmentation. For evaluation of implants and for discussion of the evidence regarding screening for implant rupture, please see the ACR Appropriateness Criteria<sup>®</sup> topic on "Breast Implant Evaluation" [17].

#### **US Breast**

There is no relevant literature to support the use of US for breast cancer screening in this clinical setting.

# Variant 5: Breast cancer screening. Transmasculine (female-to-male) patient with bilateral mastectomies ("top surgery") at any age and any risk.

Mastectomies as part of gender-affirming surgery are often subtotal, particularly in the axillary regions, to obtain an aesthetic, contoured masculine chest [1,2]. The residual breast tissue has the potential to develop malignancy. Estimation of breast cancer risk reduction in transmasculine patients following simple mastectomy is derived from high-risk cisgender women. A <2% risk of breast cancer is observed in cisgender women who undergo prophylactic mastectomy due to inherited cancer predisposition [10,27]. Hence, it is conjectured that transgender men are at a comparably very low risk of developing breast cancer after top surgery.

# **Digital Breast Tomosynthesis Screening**

There is no relevant literature to support the use of DBT for breast cancer screening in this clinical setting.

## **Mammography Screening**

There is no relevant literature to support the use of digital mammography for breast cancer screening in this clinical setting.

### **MRI Breast Without and With IV Contrast**

There is no relevant literature to support the use of MRI breast without and with IV contrast for breast cancer screening in this clinical setting.

#### **MRI Breast Without IV Contrast**

There is no relevant literature to support the use of MRI without IV contrast for breast cancer screening in this clinical setting.

#### **US Breast**

There is no relevant literature to support the use of US for breast cancer screening in this clinical setting. In cisgender women with a personal history of breast cancer, a few small and retrospective studies report utility in surveillance with US after mastectomy [28]. For a discussion of screening after mastectomy in high-risk patients, please see the ACR Appropriateness Criteria® topic on "Imaging after Mastectomy and Breast Reconstruction" [28].

# Variant 6: Breast cancer screening. Transmasculine (female-to-male) patient with reduction mammoplasty or no chest surgery, 40 years of age or older. Average-risk patient (less than 15% lifetime risk of breast cancer).

Transmasculine patients who have not undergone top surgery (and have breast tissue) have breast cancer risk comparable with cisgender women irrespective of hormone treatment [10]. For a discussion of breast cancer screening in average-risk patients, please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

### **Digital Breast Tomosynthesis Screening**

Annual screening with digital mammography or DBT is recommended in this clinical setting to screen for breast cancer beginning at age 40 and continuing while life expectancy exceeds 5 to 7 years because transmasculine patients without top surgery have breast cancer risk similar with cisgender women. Please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

In addition to planar images, DBT allows for creation and viewing of thin-section reconstructed images that decrease the lesion-masking effect of overlapping normal tissue, thereby decreasing false-positive recalls as well as improving CDR in breast cancer screening.

# **Mammography Screening**

Annual screening with digital mammography or DBT is recommended in this clinical setting to screen for breast cancer beginning at age 40 and continuing while life expectancy exceeds 5 to 7 years because transmasculine patients without top surgery have breast cancer risk similar with cisgender women. Please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

#### **MRI Breast Without and With IV Contrast**

There is no relevant literature to support the use of MRI breast without and with IV contrast for breast cancer screening in this clinical setting.

#### MRI Breast Without IV Contrast

There is no relevant literature to support the use of MRI without IV contrast for breast cancer screening in this clinical setting.

#### **US Breast**

There is insufficient evidence to support the use of US for breast cancer screening of average-risk patients with nondense breast tissue [25,29].

Dense breast tissue lowers the sensitivity of mammography and increases breast cancer risk when compared with fatty breasts [25,30]. In patients with dense breasts and no additional risk factors, breast US may be useful as an adjunct to mammography for incremental cancer detection [25,31]; however, the increased risk of a false-positive examination should be considered in the decision [25,32-34].

Variant 7: Breast cancer screening. Transmasculine (female-to-male) patient with reduction mammoplasty or no chest surgery, 30 years of age or older. Intermediate risk (patient with personal history of breast cancer, lobular neoplasia, atypical ductal hyperplasia, or 15% to 20% lifetime risk of breast cancer).

Transmasculine patients who have not undergone top surgery (and have breast tissue) have breast cancer risk comparable with eisgender women irrespective of hormone treatment [10]. Transmasculine individuals with an intermediate risk of breast cancer may benefit from beginning screening mammography earlier than 40 years of age and may also benefit from supplemental screening. For a discussion of breast cancer screening in intermediate-risk patients, please see the ACR Appropriateness Criteria<sup>®</sup> topic on "Breast Cancer Screening" [25].

# **Digital Breast Tomosynthesis Screening**

Annual screening with digital mammography or DBT is recommended in this clinical setting as it is for risk-comparable cisgender women with high-risk lesions, such as lobular neoplasia or atypical ductal hyperplasia, beginning at diagnosis but not before 30 years of age [25,35]. Transmasculine patients with a personal history of breast cancer are recommended to have mammography every 12 months because their breast cancer risk is similar to cisgender women [25,35].

The sensitivity of mammography decreases with increasing density. DBT can address some of the limitations encountered with standard digital mammography. In addition to planar images, DBT allows for creation and viewing of thin-section reconstructed images that decrease the lesion-masking effect of overlapping normal tissue, thereby decreasing false-positive recalls as well as improving CDR in breast cancer screening. Please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

#### **Mammography Screening**

Annual screening with digital mammography or DBT is recommended in this clinical setting as it is for risk-comparable cisgender women with high-risk lesions, such as lobular neoplasia or atypical ductal hyperplasia, beginning at diagnosis but not before 30 years of age [25,35]. Transmasculine patients with a personal history of breast cancer are recommended to have mammography every 12 months because their breast cancer risk is similar to cisgender women [25,35].

The sensitivity of mammography decreases with increasing density. For a discussion of breast cancer screening in intermediate-risk patients, please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

### **MRI Breast Without and With IV Contrast**

Studies of cisgender females with intermediate risk for breast cancer support the use of screening breast MRI with IV contrast in certain subsets of the population, including patients with a history of lobular neoplasia [25,36,37] or a personal history of breast cancer [25,38,39]. For a discussion of breast cancer screening in intermediate-risk patients, please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

#### **MRI Breast Without IV Contrast**

There is insufficient evidence to support the use of MRI breast without IV contrast for breast cancer screening in this clinical setting.

#### **US Breast**

In patients with dense breasts and increased risk of breast cancer, supplementing screening mammography with breast US increases cancer detection [25,40,41], although false-positives are also increased [25,40,41].

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Variant 8: Breast cancer screening. Transmasculine (female-to-male) patient with reduction mammoplasty or no chest surgery, 25 to 30 years of age or older. High risk (patient with genetic predisposition to breast cancer or untested patient with a first-degree relative with genetic predisposition to breast cancer, patient with a history of chest irradiation between 10 and 30 years of age, patient with 20% or greater lifetime risk of breast cancer).

Transmasculine patients who have not undergone top surgery (and have breast tissue) have breast cancer risk comparable with cisgender women irrespective of hormone treatment [10]. Transmasculine individuals at high risk for breast cancer include individuals with BRCA mutations and other known genetic predispositions, history of mantle radiation therapy between 10 and 30 years of age, a strong family history, or a combination of risk factors that place them at ≥20% lifetime risk of breast cancer using established risk model calculators for cisgender females [25,42]. In addition to beginning screening earlier than average-risk cisgender women, patients in this high-risk group benefit from supplemental screening.

For a discussion of breast cancer screening in high-risk patients, please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

## **Digital Breast Tomosynthesis Screening**

Annual screening with digital mammography or DBT is recommended in this clinical setting as it is for risk-comparable cisgender women beginning 8 years after radiation therapy but not before age 25 for patients who received mantle radiation between 10 and 30 years of age [25,42]. In transmasculine patients with familial breast cancer risk, an annual screening mammogram is recommended starting 10 years earlier than the affected relative's age at diagnosis but not before 30 years of age, as their breast cancer risk is similar to cisgender women [25,35].

The sensitivity of mammography decreases with increasing density. DBT can address some of the limitations encountered with standard digital mammography. In addition to planar images, DBT allows for creation and viewing of thin-section reconstructed images that decrease the lesion-masking effect of overlapping normal tissue, thereby decreasing false-positive recalls as well as improving CDR in breast cancer screening. Please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

# **Mammography Screening**

Annual screening with digital mammography or DBT is recommended in this clinical setting as it is for risk-comparable cisgender women beginning 8 years after radiation therapy but not before age 25 for patients who received mantle radiation between 10 and 30 years of age [25,42]. In transmasculine patients with familial breast cancer risk, an annual screening mammogram is recommended starting 10 years earlier than the affected relative's age at diagnosis but not before 30 years of age, as their breast cancer risk is similar to cisgender women [25,35].

#### MRI Breast Without and With IV Contrast

Evidence from studies of high-risk cisgender women supports the use of MRI breast with IV contrast for breast cancer screening in this clinical setting because transmasculine patients have breast cancer risk similar to cisgender women. Breast MRI in a high-risk population has a higher sensitivity than mammography, and the combination of mammography and MRI in this population has the highest sensitivity (92.7% compared with 52% for US and mammography combined) [25,43-50]. For this reason, MRI is recommended as an adjunct to screening DBT or mammography.

For a discussion of breast cancer screening in high-risk patients, please see the ACR Appropriateness Criteria® topic on "Breast Cancer Screening" [25].

# **MRI Breast Without IV Contrast**

There is insufficient evidence to support the use of MRI breast without IV contrast for breast cancer screening in this clinical setting.

### **US Breast**

Screening breast US may be helpful in this clinical setting because transmasculine patients have breast cancer risk similar to cisgender women. Mammography alone does not perform as well as mammography plus supplemental screening in high-risk patients, especially those with a genetic predisposition [25,40,41].

#### **Summary of Recommendations**

- Variant 1: DBT or mammography may be appropriate for breast cancer screening in an average-risk transferminine (male-to-female) patient who is 40 years of age or older with past or current hormone use for ≥5 years.
- Variant 2: DBT or mammography is usually appropriate for breast cancer screening in higher-than-average-risk transfeminine (male-to-female) patients who are 25 to 30 years of age or older with past or current hormone use for ≥5 years. Patients in this risk category have a personal history of breast cancer or chest irradiation at 10 to 30 years of age, a genetic predisposition to breast cancer, a family history of breast or ovarian cancer, or is an untested patient with a first-degree relative with a genetic predisposition to breast cancer. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- Variant 3: Imaging is usually not appropriate for breast cancer screening in an average-risk transfeminine (male-to-female) patient of any age with no hormone use or <5 years of hormone use.
- Variant 4: DBT or mammography may be appropriate for breast cancer screening in a higher-than-average-risk transfeminine (male-to-female) patient who is 25 to 30 years of age or older with no hormone use or <5 years of hormone use. Patients in this risk category have a personal history of breast cancer or chest irradiation at 10 to 30 years of age, a genetic predisposition to breast cancer, a family history of breast or ovarian cancer, or is an untested patient with a first-degree relative with a genetic predisposition to breast cancer.
- Variant 5: Imaging is usually not appropriate for breast cancer screening in a transmasculine (female-to-male) patient of any age and any risk who has had bilateral mastectomies ("top surgery").
- Variant 6: DBT or mammography is usually appropriate for breast cancer screening in an average-risk transmasculine (female-to-male) patient who is 40 years of age or older with reduction mammoplasty or no chest surgery. Patients in this risk category have <15% lifetime risk of breast cancer. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- Variant 7: DBT or mammography is usually appropriate for breast cancer screening in an intermediate-risk transmasculine (female-to-male) patient who is 30 years of age or older with reduction mammoplasty or no chest surgery. Patients in this risk category have a personal history of breast cancer, lobular neoplasia, atypical ductal hyperplasia, or a 15% to 20% lifetime risk of breast cancer. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- Variant 8: DBT or mammography is usually appropriate for breast cancer screening in a high-risk transmasculine (female-to-male) patient who is 25 to 30 years of age or older with reduction mammoplasty or no chest surgery. Patients in this risk category may have a genetic predisposition to breast cancer, a history of chest irradiation between 10 and 30 years of age, a ≥20% lifetime risk of breast cancer, or are untested patients with a first-degree relative with a genetic predisposition to breast cancer. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care). MRI with and without IV contrast is recommended as an adjunct to DBT or mammography for screening.

#### **Supporting Documents**

The evidence table, literature search, and appendix for this topic are available at <a href="https://acsearch.acr.org/list">https://acsearch.acr.org/list</a>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to <a href="https://www.acr.org/ac.">www.acr.org/ac.</a>

# **Appropriateness Category Names and Definitions**

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

## **Relative Radiation Level Information**

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria. Radiation Dose Assessment Introduction document [51].

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
0	0 mSv	0 mSv
<b>€</b>	<0.1 mSv	<0.03 mSv
<b>⊕⊕</b>	0.1-1 mSv	0.03-0.3 mSv
<b>⊕⊕</b>	1-10 mSv	0.3-3 mSv
❖❖❖❖	10-30 mSv	3-10 mSv
❖❖❖❖❖	30-100 mSv	10-30 mSv

<sup>\*</sup>RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.