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# Oncotype DX for Comprehensive Treatment in Male Breast Cancer: A Case Report and Literature Review

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**Abstract**

Male breast cancer (MBC) is uncommon in clinical practice. Using the 21-gene assay to facilitate decision-making on comprehensive treatment of MBC is rarely reported. This study reports the case of a 53-year-old man with left breast cancer. Modified radical mastectomy was performed. Endocrine treatment was chosen for the patient according to the result of the 21-gene assay, a recommended genomic test of breast cancer. The patient remained in good health without evidence of recurrence at 18-month follow-up. This case provides a reference mode for the comprehensive management of early-stage, estrogen receptor–expressing and lymph node–negative MBC patients.

**Keywords**

male breast cancer, oncotype DX, endocrine therapy, treatment

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Male breast cancer (MBC) is rare in clinical practice. On a global scale, MBC accounts for less than 1% of all breast cancers (BCs) and less than 1% of male cancers (Siegel, Miller, & Jemal, 2018). In China, MBC represents 1.4% of all new cases of BC (Chen et al., 2016). The onset age of MBC is about 60–70 years (Ottini, 2014). The pathogenesis of MBC has not been clearly studied. The risk factors for MBC are mainly age, race, obesity, alcohol consumption, gene mutation, radiation exposure, abnormal expression of hormone receptors, disease in liver or testis, Klinefelter's syndrome, and so forth. (Brinton et al., 2014). About 15%–20% of MBC patients have a family history of breast or ovarian cancer and 10% have a genetic predisposition. BRCA2 is the strongest gene correlated with MBC (Silvestri et al., 2016).

Since most of the data on MBC therapy comes from single-center studies, the treatment of MBC largely follows patterns that have been set for the management of postmenopausal female breast cancer (FBC). Overtreatment with chemotherapy is a significant concern among patients and physicians. It is a complex and long-term task to provide male patients with reasonable and standardized management.

The eighth edition of the American Joint Committee on Cancer (AJCC), the cancer staging manual, is effective from January 1, 2018, in which the clinical utility of Oncotype DX is mentioned as part of cancer staging for the first time and has received widespread attention (Greene et al., 2016). More rational technic and algorithmic approaches that predict recurrence risk are evolving (Bryant, Fisher, Gunduz, Costantino, & Emir, 1998; Esteva & Hortobagyi, 2004; Hayes, 2000; Henderson & Patek, 1998). Paik and his team selected 250 genes from DNA arrays, genomic databases, and published literature (Cronin et al., 2004; Golub et al., 1999; Perou et al., 2000; Sorlie et al., 2001; van't Veer et al., 2002) and analyzed the relationship of their expression level and recurrence from three clinical studies (Cobleigh et al., 2003; Esteban et al., 2003; Paik et al., 2003). Subsequently, they selected 16 cancer-related genes and 5 reference genes and designed an algorithm to evaluate the corresponding recurrence score

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(RS) of each sample. As a genomic test, Oncotype DX has been proven to have a predictive effect on clinical outcomes. Clinical guidance including from both the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) recommend Oncotype DX for helping adjuvant therapy decision-making to avoid overtreatment (NCCN, 2014).

As the treatment of MBC is currently managed in a similar fashion to FBC, using Oncotype DX in early-stage, estrogen receptor (ER)–expressing and lymph node (LN)–negative MBC patients makes sense. However, there are no validation studies in this cohort. In the individualized treatment of MBC, few cases were reported to rely on Oncotype DX and make a therapy decision to avoid overtreatment with chemotherapy (Paik et al., 2004; Wajeeha, Takemi, & Mohammad, 2016; Yokoyama, Kobayashi, Nakamura, & Nakajima, 2012). However, previous case reports of Oncotype DX in MBC focused on the process of therapeutic decision and lacked follow-up data.

Herein, a case of the 21-gene assay used for therapeutic decision-making in MBC is reported. Treatment advances in MBC, Oncotype DX in MBC, pros and cons of Oncotype DX, and current usage in Chinese population are reviewed. The report highlight that Oncotype DX may be a considerable approach for MBC patients.

## Case Report

### *Presentation and Diagnosis*

In April 2017, a 53-year-old Chinese male with no family history of breast or ovarian cancer attended the hospital, complaining of a tender mass in the outer left breast region. The patient noted the mass 1 month ago, but it had persisted with no improvement in symptoms. He was diagnosed with hypopharyngeal cancer one and a half years earlier. He also previously had a total laryngectomy and a bilateral cervical LN dissection, followed by 25 sessions of radiotherapy. The last session of radiotherapy was in December 2016. He achieved satisfactory disease control and remission. Social history included being an occasional drinker, but he denied ever smoking. Physical exam reported symmetrical breasts with no nipple discharge and retraction, skin ulcers, or orange-peel appearance. No masses were palpated in the right breast, but there was a relatively firm, mobile mass measuring ~1.5 × 1.0 cm at the areolar border laterally in the left breast. There were no palpable axillary or supraclavicular nodes bilaterally. Mammogram reported a 1.48 × 1.15 cm mass with irregular margins at the areolar border laterally in the left breast, 1.2 cm from the nipple (Breast Imaging – Reporting And Data System (BI-RADS) 4C; Figure 1a). Ultrasound imaging clearly demonstrated a hypoechoic mass measuring ~1.18 × 0.71 × 0.58 cm at the 3 o'clock position in the left breast (BI-RADS 4C; distance from skin: 0.25 cm; maximum value of elastic modulus: 140.8 kPa; average value: 64.2 kPa). The mass was lobulated with an unclear edge and rich bloodstream signals within and close to the mass. No obvious sonographic evidence of enlarged LNs was found in bilateral axils, neck, and supraclavicular and subclavian regions (Figure 1b–d). Ultrasound-guided core needle biopsy (UG-CNB) was performed and pathological diagnosis was invasive carcinoma (Figure 2a).

### *Surgery, Oncotype DX, and Adjuvant Treatment*

After discussing treatment options with the patient and further discussing with other breast surgeons, modified radical mastectomy of left breast was performed. The tumor was dissected postoperatively in the left mastectomy specimen. The mass was about 1.35 × 0.85 × 0.65 cm, hard, gray in section, slightly wrinkled, without capsule or obvious burrs around. Seven LNs of level I and four LNs of level II were removed. The postoperative pathology was invasive carcinoma of left breast (histological grade II; T1N0M0; T: Tumor, N: Node, M: metastasis; Figure 2b). Immunohistochemical analysis was identified as follows: CK5/6 (−), P63 (−), ER (90%+), PR (75%+), HER-2 (1+), E-cadherin (+), GATA-3 (+), Ki-67 (10 %+), P120 (+) (Figure 2B). All LNs were negative for metastatic carcinoma (Figure 2c).

Then the 21-gene assay was recommended for the patient. The 21 genes were divided into several groups based on their types and main functions, including proliferation, invasion, estrogen, HER-2 group, reference group, and others (Figure 3a). RS can be calculated according to the following formula: RS = +0.47 × HER-2 group score − 0.34 × estrogen group score + 1.04 × proliferation group score + 0.10 × invasion group score + 0.05 × CD68 − 0.08 × GSTM1 − 0.07 × BAG1. According to the RS value, patients can be divided into three categories, including low risk (RS $<18$), moderate risk ($18 \leq$ RS $< 31$), and high risk (RS $\geq 31$). The overexpression of advantageous genes (estrogen group, GSTM1, and BAG1) may result in a lower RS value, while overexpression of disadvantageous genes (proliferation group, HER-2 group, invasion group, and CD68) may result in a higher RS value.

Reverse transcription polymerase chain reaction was performed to detect the expression of 21 genes in tumor tissues. In this case, RS was calculated based on the expression results. RS value of the patient was 15.9213. The results demonstrated the 10-year risk of recurrence and metastasis was 9% (95% CI [7%, 10%]) and benefit rate from chemotherapy might be lower than 10% (Figure

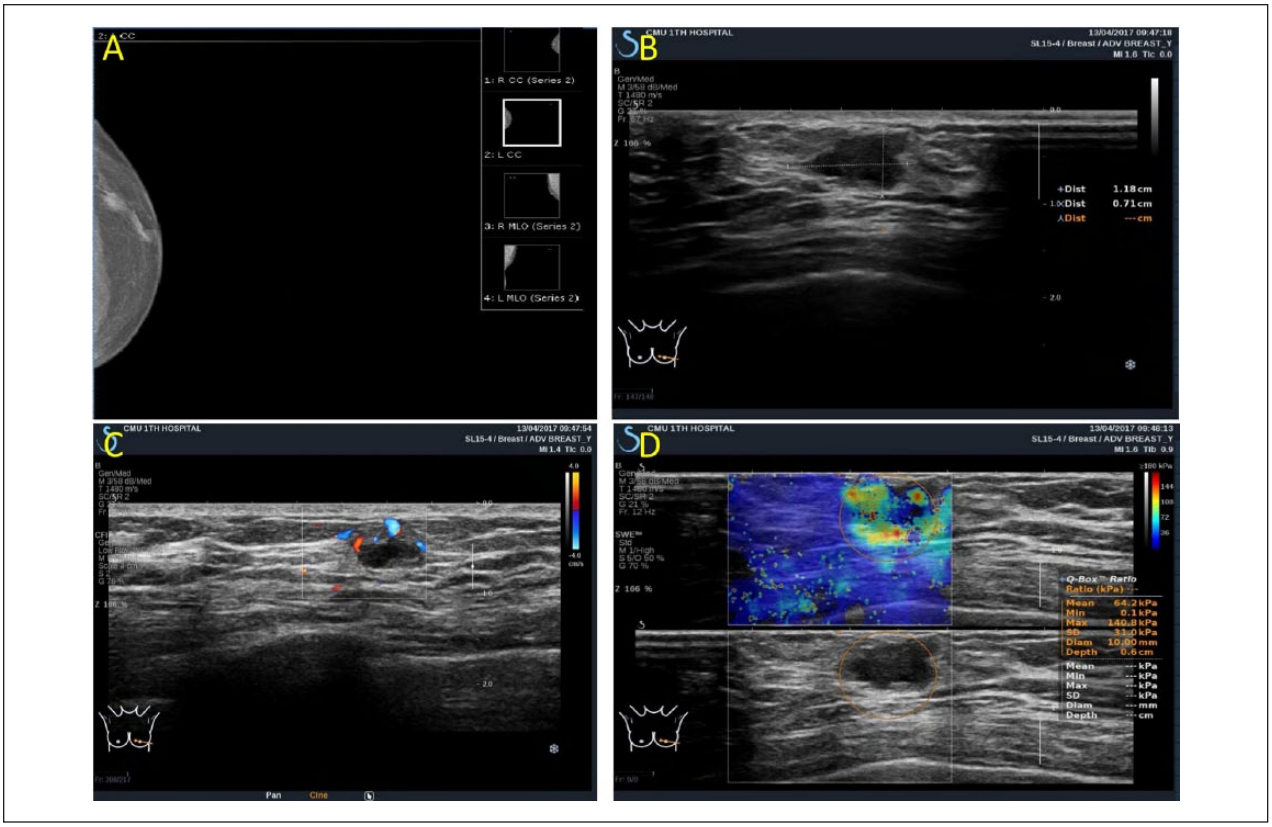


**Figure 1.** Mammogram and ultrasound imaging of the patient. (a) Mammogram shows a 1.48 × 1.15 cm mass in the left breast Breast Imaging – Reporting And Data System (BI-RADS 4C). (b) Ultrasound imaging shows a hypoechoic mass measuring ~1.18 × 0.71 × 0.58 cm in the left breast. (c) Color Doppler flow imaging (CDFI) shows rich bloodstream signals within and close to the mass. (d) The maximum elastic modulus of the mass is 140.8 kPa and the average elastic modulus is 64.2 kPa.

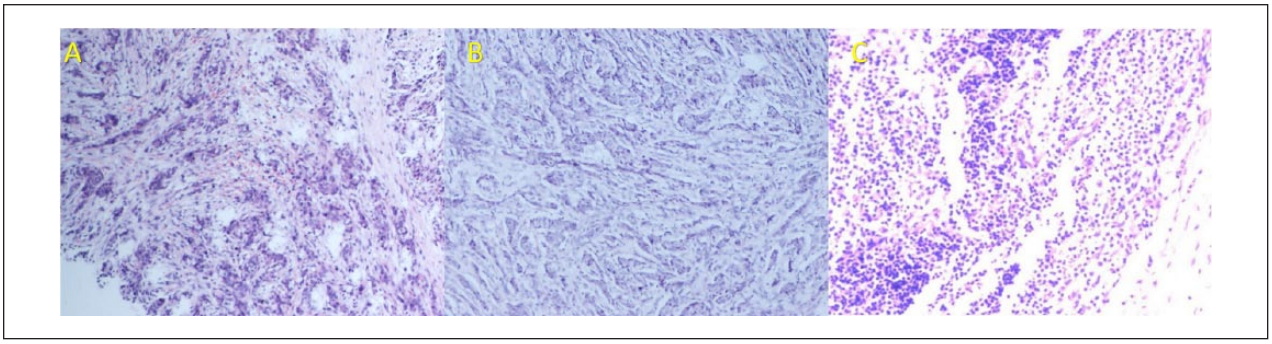


**Figure 2.** Pathology results of the patient. (a) Pathological diagnosis of ultrasound-guided core needle biopsy (UG-CNB) is invasive carcinoma. (b) The postoperative pathology is invasive carcinoma (histological grade II). (c) All lymph nodes are negative for metastatic carcinoma.

3b–d). Based on the results already mentioned, using endocrine drug tamoxifen (TAM) alone for 5 years was chosen as the adjuvant treatment scheme. The postoperation course was uneventful, and the patient continued medical follow-up with our department. He was followed up with breast Doppler ultrasound examinations every 3 months and mammogram twice a year and remained in good health without evidence of recurrence at the 1.5-year follow-up.

## Discussion

Compared with FBC, MBC is usually diagnosed at a later stage, with larger tumors, more LN metastasis, lower

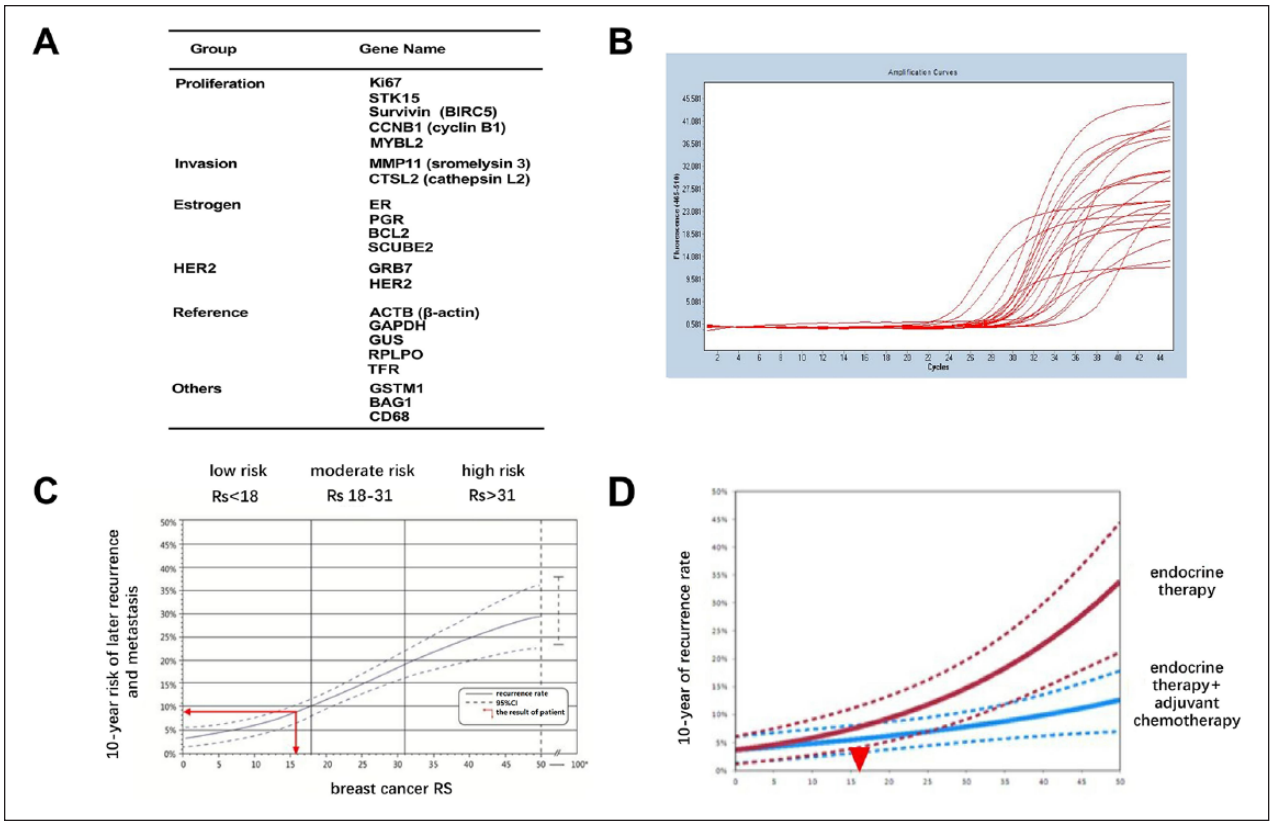


**Figure 3.** The 21-gene assay results of the patient. (a) The composition of the 21-gene assay. (b) Reverse transcription polymerase chain reaction results of the 21-gene assay. (c) The relationship between recurrence score (RS) and 10-year risk of recurrence and metastasis in the 21-gene assay. The 10-year risk of recurrence and metastasis was 9%. (d) The relationship between RS and 10-year recurrence risk under different treatment regimens. The benefit rate of the patient from chemotherapy was lower than 10%.

positive rate of Her-2 and higher positive rate of ER (Abhyankar, Hoskins, Abern, & Calip, 2017; Chavez-Macgregor, Clarke, Lichtensztajn, Hortobagyi, & Giordano, 2013; Khan, Allerton, & Pettit, 2015).

## *Progress in the Treatment of MBC*

Multidisciplinary and comprehensive treatment demonstrate better results in MBC. The most common operative method of MBC patients is modified radical mastectomy. Sentinel lymph node biopsy is also applied to avoid unnecessary LN dissection and reduce complications (Port, Fey, Cody, & Borgen, 2001). Chemotherapy is commonly used in MBC, with the same indications as in FBC (Cihan, 2014). Postoperative adjuvant chemotherapy can significantly improve the overall survival (OS) rate and reduce the local recurrence rate of MBC patients with positive LN metastasis (Di Lauro et al., 2015; Nwashilli & Ugiagbe, 2015). Postoperative radiotherapy standard for MBC is still established in accordance with FBC, with a total of 25 sessions and 2 Gy/session of dose (Bratman, Kapp, & Horst, 2012; Eggemann et al., 2013). Endocrine therapy plays an important role in MBC treatment. TAM is used as a first-line hormone in MBC endocrine treatment, to prolong disease-free survival and OS, with a normal dose of 20 mg/day, for 5 years (Khan et al., 2015).

## *Oncotype DX in MBC*

A few cases reported that Oncotype DX was used as a decision-making tool and overtreatment was avoided in MBC patients (Paik et al., 2004; Wajeeha et al., 2016; Yokoyama et al., 2012). However, previous case reports focused on the process of therapeutic decision. Massarweh analyzed a total of 3,806 men with ER-positive BC. Five-year breast cancer-specific survival (BCSS) and OS were available from the Surveillance, Epidemiology, and End Results (SEER) program for 322 men. The large genomic study reported that men with lower RS results had lower mortality from ER-positive BC, and many could be spared the risks associated with overtreatment, particularly

chemotherapy (Massarweh et al., 2018). Another large genomic study of 347 MBC patients drew similar conclusions (Shak et al., 2009). Furthermore, MBCs were discovered to display similar gene signatures and distribution of genomic expression as FBCs (Grenader et al., 2014; Shak et al., 2009). Compared with some clinical pathology factors, Oncotype DX is more reliable in predicting risk of distant metastasis in ER-expressing and LN-negative patients. Because of the similar distribution of genomic signatures, Oncotype DX may be a considerable approach for MBC to assess the recurrence risk.

## *Pros and Cons of Oncotype DX*

Oncotype DX can acquire effective information directly from formalin-fixed paraffin-embedded (FFPE) tissues, which available (Paik et al., 2004). Oncotype DX provides credible prediction of distant recurrence risk in FBC. The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14 reported that distant recurrence rate of the low-risk group was significantly lower than that of the high-risk group ($p < .001$) and this proved that RS could predict clinical outcome more accurately, compared with classical clinical pathology markers (Fisher et al., 1989, 2004). NSBAP B-20 affirmed that using Oncotype DX to distinguish patients with high- or low-recurrence risk has guiding significance for whether adjuvant chemotherapy should be selected (Fisher et al., 1997, 2004). A phase III clinal trial, the Trial Assigning Individualized Options for Treatment (TAILORx), suggested that with age >50 years and RS ≤25 and age ≤50 years and RS ≤15, chemotherapy was omissible for ER-positive, HER-2 negative, and LN-negative FBC patients (Sparano et al., 2018). Albain and Dowsett obtained a similar result that a high-risk group could benefit from chemotherapy, while a low-risk group could not (Albain et al., 2010; Dowsett et al., 2010). In 2015, Genomic Health released advanced results that Oncotype DX was also suitable for FBC patients with positive ER, negative HER-2, and lymphatic metastasis (less than 3 LNs; Jennifer, Jeffery, & Calvin, 2015). The reference studies in this paragraph included FBC patients only.

Oncotype DX also has limitations. Several researches reported that age might be an important factor in the evaluation of prognosis. More detailed studies on the association between age and Oncotype DX are required (Sparano et al., 2018). Furthermore, Oncotype DX mainly focuses on classical chemotherapy. It is difficult to assess the applicability of the 21-gene assay in new chemotherapy strategies. Besides, there are clinical challenges concerning Oncotype DX, such as slow concordance of risk assignment by different tests, inaccurate prediction of late recurrences, and poor prediction of drug-specific or regimen-specific benefits (Prat et al., 2012).

## *Historical and Current Usage of Oncotype DX in the Chinese Population*

The indications of the 21-gene assay in China are rarely reported. For Chinese patients, Oncotype DX is still limited in practice. The Oncotype DX test kit is so expensive that some patients choose chemotherapy directly. With the development of Chinese products, some hospitals have built excellent platforms to perform the 21-gene assay for BC patients. The assay is based on liquid-phase chip techniques, and the diagnostic cost of each assay has been dropping to around 5,000 RMB.

Early detection, diagnosis, and treatment are important factors affecting the prognosis of MBC. More clinical trials at the genomic level might provide new ideas for the future study of MBC (Fostira et al., 2018). Besides Oncotype DX, multigene tests based on high-throughput technology platforms, innovative prediction models based on interdisciplinary research, and dynamic risk monitoring based on repetitive tests will offer new opportunities and directions for multigene tests of MBC in the future.

## Declaration of Conflicting Interests

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## Ethics Approval and Informed Consent Statements

This study was approved by the Ethics Committee of the First Affiliated Hospital of China Medical University (Approval number. AF-SOP-07-1.1-01). All procedures performed in the study were in accordance with the ethical standards of the institutional and national research committee and with the Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the patient for the publication of this case report. The patient signed on the consent, which was maintained properly by the China Medical University.

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## References

Abhyankar, N., Hoskins, K. F., Abern, M. R., & Calip, G. S. (2017). Descriptive characteristics of prostate cancer in patients with a history of primary male breast cancer – A

SEER analysis. *BMC Cancer*, *17*(1), 659. doi:10.1186/s12885-017-3640-7

Albain, K. S., Barlow, W. E., Shak, S., Hortobagyi, G. N., Livingston, R. B., Yeh, I. T., … Hayes, D. F. (2010). Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: A retrospective analysis of a randomised trial. *Lancet Oncology*, *11*(1), 55–65. doi:10.1016/s1470-2045(09)70314-6

Bratman, S. V., Kapp, D. S., & Horst, K. C. (2012). Evolving trends in the initial locoregional management of male breast cancer. *Breast*, *21*(3), 296–302. doi:10.1016/j.breast.2012.01.008

Brinton, L. A., Cook, M. B., McCormack, V., Johnson, K. C., Olsson, H., Casagrande, J. T., … Thomas, D. B. (2014). Anthropometric and hormonal risk factors for male breast cancer: Male breast cancer pooling project results. *Journal of the National Cancer Institute*, *106*(3), djt465. doi:10.1093/jnci/djt465

Bryant, J., Fisher, B., Gunduz, N., Costantino, J. P., & Emir, B. (1998). S-phase fraction combined with other patient and tumor characteristics for the prognosis of node-negative, estrogen-receptor-positive breast cancer. *Breast Cancer Research and Treatment*, *51*(3), 239–253. doi:10.1023/a:1006184428857

Chavez-Macgregor, M., Clarke, C. A., Lichtensztajn, D., Hortobagyi, G. N., & Giordano, S. H. (2013). Male breast cancer according to tumor subtype and race: A population-based study. *Cancer*, *119*(9), 1611–1617. doi:10.1002/cncr.27905

Chen, W., Zheng, R., Baade, P. D., Zhang, S., Zeng, H., Bray, F., … He, J. (2016). Cancer statistics in China, 2015. *A Cancer Journal for Clinicians*, *66*(2), 115–132. doi:10.3322/caac.21338

Cihan, Y. B. (2014). Relationship of body mass index with prognosis in breast cancer patients treated with adjuvant radiotherapy and chemotherapy. *Asian Pacific Journal of Cancer Prevention*, *15*(10), 4233–4238.

Cobleigh, M. A., Bitterman, P., Baker, J., Cronin, M., Liu, M., Borchik, R., … Liu, L. (2003). Tumor gene expression predicts distant disease-free survival (DDFS) in breast cancer patients with 10 or more positive nodes: High throughout RT-PCR assay of paraffin-embedded tumor tissues. *Proceedings of the American Society of Clinical Oncology*, *22*, 850.

Cronin, M., Pho, M., Dutta, D., Stephans, J. C., Shak, S., Kiefer, M. C., … Baker, J. B. (2004). Measurement of gene expression in archival paraffin-embedded tissues-development and performance of a 92-gene reverse transcriptase-polymerase chain reaction assay. *American Journal of Pathology*, *164*(1), 35–42. doi:10.1016/s0002-9440(10)63093-3

Di Lauro, L., Pizzuti, L., Barba, M., Sergi, D., Sperduti, I., Mottolese, M., … Maugeri-Sacca, M. (2015). Efficacy of chemotherapy in metastatic male breast cancer patients: A retrospective study. *Journal of Experimental & Clinical Cancer Research*, *34*, 26. doi:10.1186/s13046-015-0143-8

Dowsett, M., Cuzick, J., Wale, C., Forbes, J., Mallon, E. A., Salter, J., … Shak, S. (2010). Prediction of risk of distant recurrence using the 21-gene recurrence score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: A TransATAC study. *Journal of Clinical Oncology*, *28*(11), 1829–1834. doi:10.1200/jco.2009.24.4798

Eggemann, H., Ignatov, A., Stabenow, R., von Minckwitz, G., Rohl, F. W., Hass, P., & Costa, S. D. (2013). Male breast cancer: 20-year survival data for post-mastectomy radiotherapy. *Breast Care (Basel)*, *8*(4), 270–275. doi:10.1159/000354122

Esteban, J., Backer, J., Cronin, M., Liu, M.-L., Llamas, M. G., Walker, M. G., … Shak, S. (2003). Tumor gene expression and prognosis in breast cancer: Multi-gene RT-PCR assay of paraffin-embedded tissue. *Proceedings of the American Society of Clinical Oncology*, *22*, A3416.

Esteva, F. J., & Hortobagyi, G. N. (2004). Prognostic molecular markers in early breast cancer. *Breast Cancer Research*, *6*(3), 109–118. doi:10.1186/bcr777

Fisher, B., Costantino, J., Redmond, C., Poisson, R., Bowman, D., Couture, J., … Ketner, M. (1989). A randomized clinical-trial evaluating tamoxifen in the treatment of patients with node-negative e breast cancer who have oestrogen-receptor positive tumors. *New England Journal of Medicine*, *320*(8), 479–484. doi:10.1056/nejm198902233200802

Fisher, B., Dignam, J., Wolmark, N., DeCillis, A., Emir, B., Wickerham, D. L., … Margolese, R. G. (1997). Tamoxifen and chemotherapy for lymph node-negative, estrogen receptor-positive breast cancer. *JNCI-Journal of the National Cancer Institute*, *89*(22), 1673–1682. doi:10.1093/jnci/89.22.1673

Fisher, B., Jeong, J. H., Bryant, J., Anderson, S., Dignam, J., Fisher, E. R., & Wolmark, N. (2004). Treatment of lymph-node-negative, oestrogen-receptor-positive breast cancer: Long-term findings from National Surgical Adjuvant Breast and Bowel Project randomised clinical trials. *Lancet*, *364*(9437), 858–868. doi:10.1016/s0140-6736(04)16981-x

Fostira, F., Saloustros, E., Apostolou, P., Vagena, A., Kalfakakou, D., Mauri, D., … Konstantopoulou, I. (2018). Germline deleterious mutations in genes other than BRCA2 are infrequent in male breast cancer. *Breast Cancer Research and Treatment*, *169*(1), 105–113. doi:10.1007/s10549-018-4661-x

Golub, T. R., Slonim, D. K., Tamayo, P., Huard, C., Gaasenbeek, M., Mesirov, J. P., … Lander, E. S. (1999). Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring. *Science*, *286*(5439), 531–537. doi:10.1126/science.286.5439.531

Greene, F. L., Page, D. L., Fleming, I. D., Fritz, A. G., Balch, C. M., Haller, D. G., & Morrow, M. (Eds.). (2016). *AJCC cancer staging manual* (8th ed.). New York, NY: Springer.

Grenader, T., Yerushalmi, R., Tokar, M., Fried, G., Kaufman, B., Peretz, T., & Geffen, D. B. (2014). The 21-gene recurrence score assay (Oncotype DX) in estrogen receptor-positive male breast cancer: Experience in an Israeli cohort. *Oncology*, *87*(1), 1–6. doi:10.1159/000360793

Hayes, D. F. (2000). Do we need better prognostic factors in node-negative breast cancer? Arbiter. *European Journal of Cancer*, *36*(3), 302–306. doi:10.1016/s0959-8049(99)00303-2

Henderson, I. C., & Patek, A. J. (1998). The relationship between prognostic and predictive factors in the management of breast cancer. *Breast Cancer Research and Treatment*, *52*(1–3), 261–288. doi:10.1023/a:1006141703224

Jennifer, R., Jeffery, P., & Calvin, Y. (2015). Effect of the 21-gene RT-PCR assay on treatment administered in early-stage, node-positive (N+) breast cancer. *Journal of Clinical Oncology*, *33*, e11510.

Khan, M. H., Allerton, R., & Pettit, L. (2015). Hormone Therapy for Breast Cancer in Men. *Clinical Breast Cancer*, *15*(4), 245–250. doi:10.1016/j.clbc.2015.01.007

Massarweh, S. A., Sledge, G. W., Miller, D. P., McCullough, D., Petkov, V. I., & Shak, S. (2018). Molecular characterization and mortality from breast cancer in men. *Journal of Clinical Oncology*, *36*(14), 1396–1404. doi:10.1200/jco.2017.76.8861

National Comprehensive Cancer Network. (2014). *NCCN clinical practice guidelines in oncology: Breast cancer version 3 [EB/OL]*.

Nwashilli, N. J., & Ugiagbe, E. E. (2015). Bilateral synchronous male breast cancer. *Saudi Medical Journal*, *36*(3), 359–362. doi:10.15537/smj.2015.3.10109

Ottini, L. (2014). Male breast cancer: A rare disease that might uncover underlying pathways of breast cancer. *Nature Reviews Cancer*, *14*(10), 643–644. doi:10.1038/nrc3806

Paik, S., Shak, S., Tang, G., Kim, C., Baker, J., Cronin, M., … Park, T. (2003). Multi-gene RT-PCR assay for predicting recurrence in node negative breast cancer patients—NSABP studies B-20 and B-14. *Breast Cancer Research and Treatment*, *82*, A16.

Paik, S., Shak, S., Tang, G., Kim, C., Baker, J., Cronin, M., & … Wolmark, N. (2004). A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *New England Journal of Medicine*, *351*(27), 2817–2826. doi:10.1056/NEJMoa041588

Perou, C. M., Sorlie, T., Eisen, M. B., van de Rijn, M., Jeffrey, S. S., Rees, C. A., … Botstein, D. (2000). Molecular portraits of human breast tumours. *Nature*, *406*(6797), 747–752. doi:10.1038/35021093

Port, E. R., Fey, J. V., Cody, H. S., & Borgen, P. I. (2001). Sentinel lymph node biopsy in patients with male breast carcinoma. *Cancer*, *91*(2), 319–323.

Prat, A., Parker, J. S., Fan, C., Cheang, M. C., Miller, L. D., Bergh, J., … Perou, C. M. (2012). Concordance among gene expression-based predictors for ER-positive breast cancer treated with adjuvant tamoxifen. *Annals of Oncology*, *23*(11), 2866–2873. doi:10.1093/annonc/mds080

Shak, S., Palmer, G., Baehner, F. L., Millward, C., Watson, D., & Sledge, G. W. (2009). Molecular characterization of male breast cancer by standardized quantitative RT-PCR analysis: First large genomic study of 347 male breast cancers compared to 82,434 female breast cancers. *Journal of Clinical Oncology*, *27*, 549.

Siegel, R. L., Miller, K. D., & Jemal, A. (2018). Cancer statistics, 2018. *A Cancer Journal for Clinicians*, *68*(1), 7–30. doi:10.3322/caac.21442

Silvestri, V., Barrowdale, D., Mulligan, A. M., Neuhausen, S. L., Fox, S., Karlan, B. Y., … Ottini, L. (2016). Male breast cancer in BRCA1 and BRCA2 mutation carriers: Pathology data from the Consortium of Investigators of Modifiers of BRCA1/2. *Breast Cancer Research*, *18*(1), 15. doi:10.1186/s13058-016-0671-y

Sorlie, T., Perou, C. M., Tibshirani, R., Aas, T., Geisler, S., Johnsen, H., … Borresen-Dale, A. L. (2001). Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proceedings of the National Academy of Sciences of the United States of America*, *98*(19), 10869–10874. doi:10.1073/pnas.191367098

Sparano, J. A., Gray, R. J., Makower, D. F., Pritchard, K. I., Albain, K. S., Hayes, D. F., … Sledge, G. W., Jr. (2018). Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. *New England Journal of Medicine*, *379*(2), 111–121. doi:10.1056/NEJMoa1804710

van't Veer, L. J., Dai, H., van de Vijver, M. J., He, Y. D., Hart, A. A. M., Mao, M., & … Friend, S. H. (2002). Gene expression profiling predicts clinical outcome of breast cancer. *Nature*, *415*(6871), 530–536. doi:10.1038/415530a

Wajeeha, R., Takemi, T., & Mohammad, A. R. (2016). Treating male breast cancer: Role of Oncotype Dx in early stage male breast cancer patients. A case series and review of literature. *Clinical Case Reports and Reviews*, *2*(2), 344–346. doi:10.15761/CCRR.1000210

Yokoyama, J., Kobayashi, T., Nakamura, T., & Nakajima, Y. (2012). A case of male breast cancer in which oncotype DX was used to determine the therapeutic strategy. *Gan To Kagaku Ryoho*, *39*(12), 2057–2059.