



But it's MY Body: Breast Cancer Risks and Decision Making

March 26, 2018

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Conflict of Interest

- **Dr. Pederson serves as a consultant for Myriad Genetics, Inc.**

Practice of Clinical Cancer Genetics

- When faced with a patient with cancer:
 - Is it heritable?
 - Is it sporadic?
- Implications for patient
 - Which cancer(s) is this patient at risk for?
 - At what ages do these risks rise?
 - What to do for the patient?
- Implications for patient's family
 - Who are at risk for cancer?
 - What to do for each family member?

The Story of Rachel Cowden (ca 1960' s)

- Rachel Cowden Died at 33 Years of Age
 - ❑ Metastatic Breast Cancer
 - ❑ Population Average Age at Diagnosis of Breast Cancer: 60 Years Old
- Ms Cowden also had Unusual Skin Findings, Thyroid Neoplasias, etc
 - ❑ No doctor knew what she had (1963)
- The New Disorder was Named in Honor of Rachel Cowden (by Lloyd & Denis, *Ann Intern Med* 1963)
 - ❑ Cowden Syndrome

PTEN- Associated Age-Related Cancer Risks Help Guide Management

Cancer	General population risk	Lifetime Risk in CS with <i>PTEN</i> mutation
Breast	12%	85%
Thyroid	1%	35%
Endometrial	2.6%	28%
Renal cell	1.6%	34%
Colon	5%	9%
Melanoma	2%	6%

PTEN mutations Increase the Risk of Early-Onset Breast Cancer

	By age 50	Lifetime Risk
Population Risk	2%	7-12%
Hereditary Risk	Up to 50%	67-85%



Tan et al. Clin Cancer Res 2012; 18(2): 400-407
Bubien V et al. J Med Genet 2013; 50(4): 255-63
Nieuwenhuis MH et al. Fam Cancer 2013; 13(1): 1818-24

Breast cancer is often diagnosed again

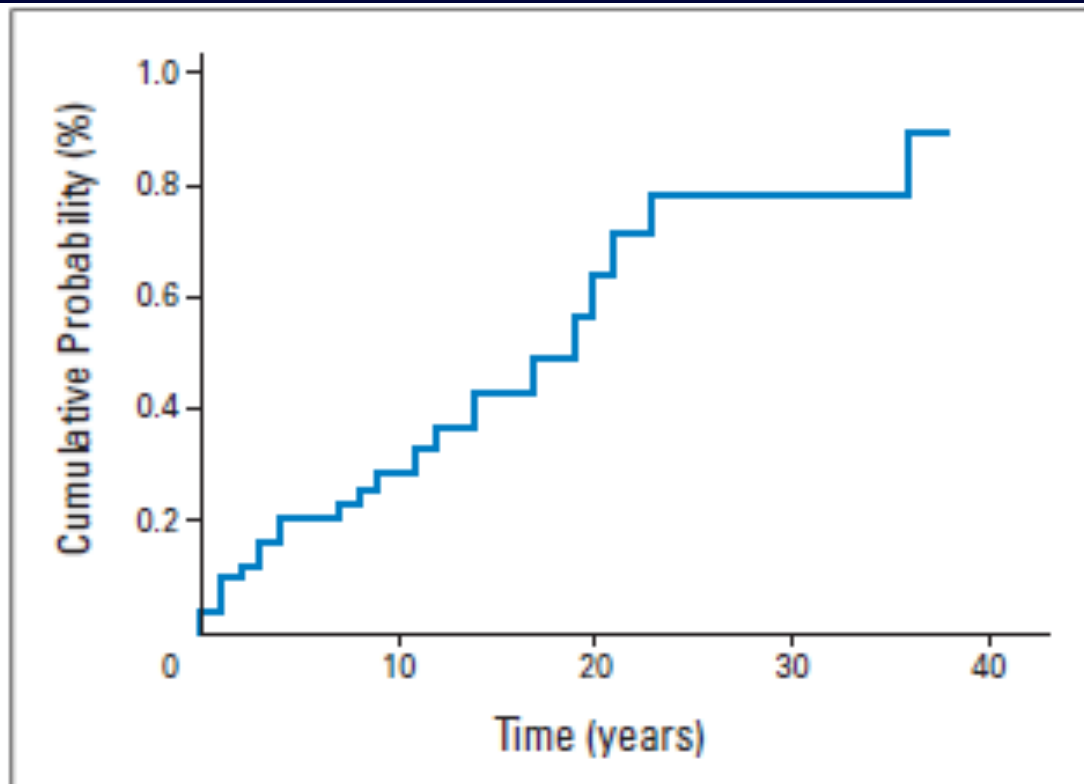


Fig 2. Cumulative risk of breast second malignant neoplasm after first breast cancer in patients with *PTEN* hamartoma tumor syndromes.

Current NCCN Guidelines for PHTS

Breast Management

- **Breast awareness starting at age 18 y**
- **Clinical breast exam every 6-12 months, starting at age 25, or 5-10 years before the earliest known breast cancer in the family**
- **Annual mammography with consideration of tomosynthesis and breast MRI screening starting at age 30-35 until age 75**
- **Consider risk-reducing mastectomy**

Why MRI?

More DCIS and smaller node negative cancers

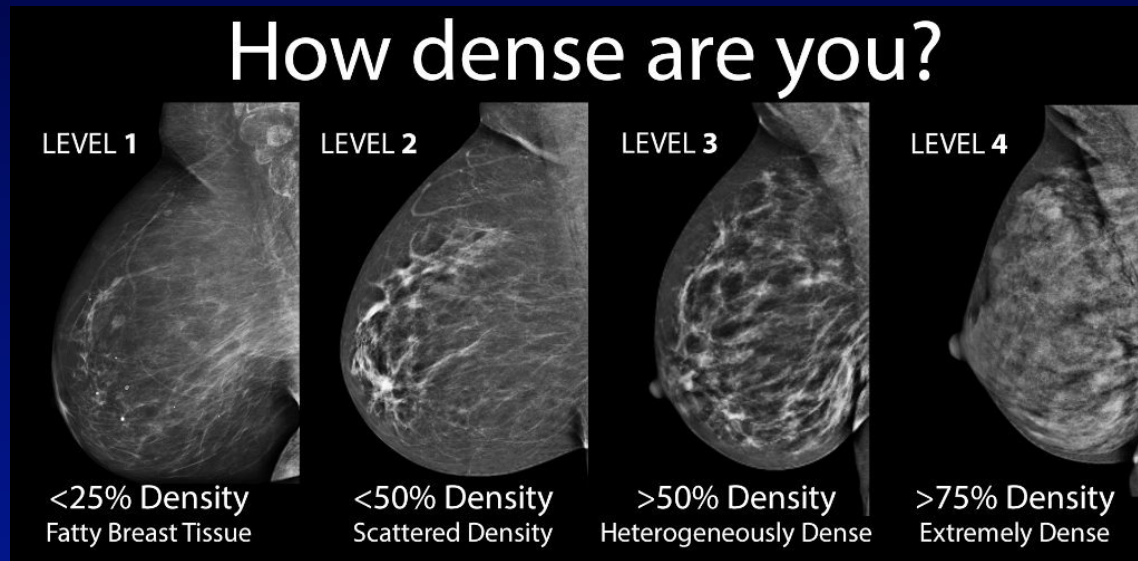
- Prospective, not randomized
- 445 mammo + MRI
- 830 mammo only
- Mean F/U: 3 years

Type of cancer	HR (+MRI)
DCIS	1.71
Invasive cancer	0.79
< 2cm, LN-	1.33
> 2 cm , LN+	0.30
	P=0.008

Warner et al. JCO 2011; 29: 1664-1669.

What about Digital Breast Tomosynthesis – 3D mammography?

- **Density can mask tumors**
- **25-40% improved sensitivity**
- **15% fewer false positives**
- **No data specifically in PTEN carriers**



Friedewald et al. JAMA 2014; 311: 2499-2507

Risk Reducing Mastectomy

OCCULT BREAST CANCER RISK: ~3%



BREAST CANCER RISK REDUCTION

Consider skin-sparing, nipple-sparing
bilateral risk-reducing mastectomy



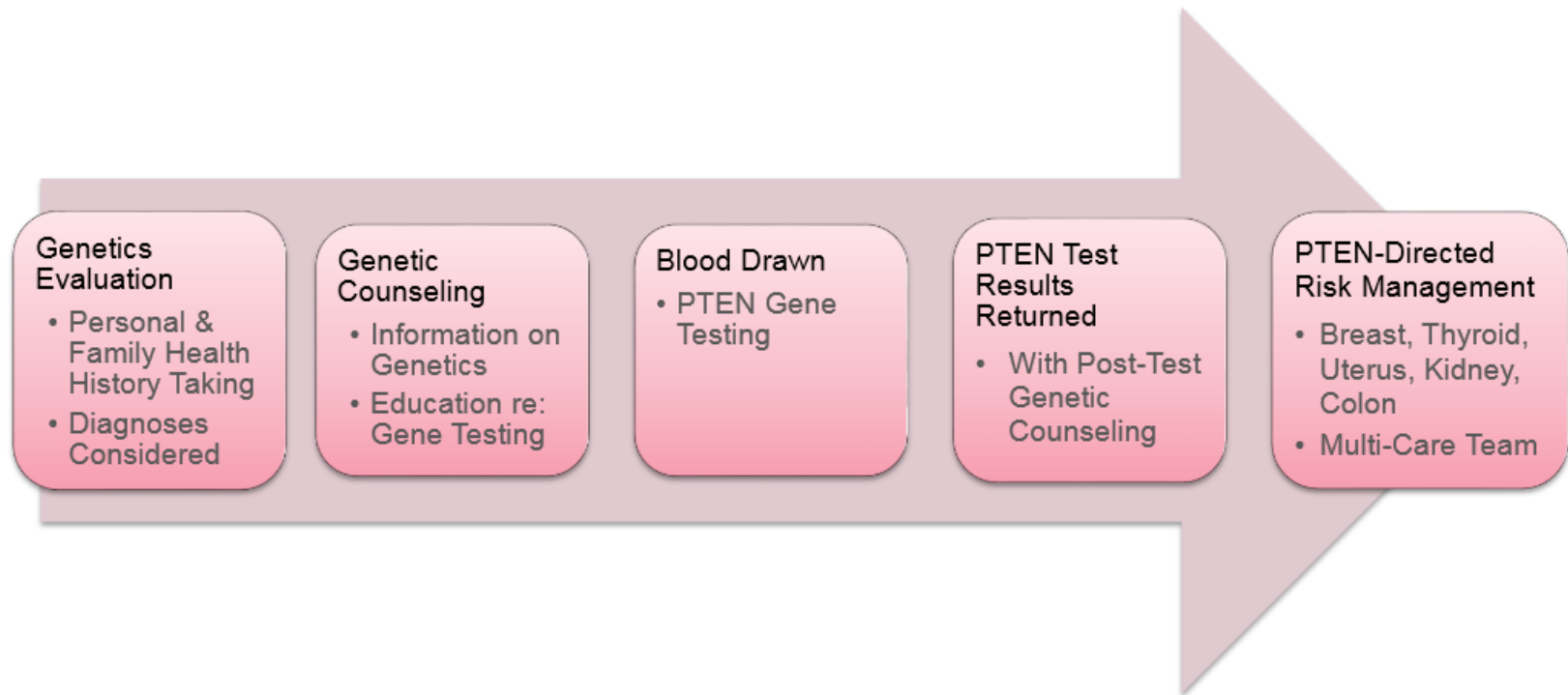
1. Domchek SM, et al. Association of Risk-Reducing Surgery in BRCA1 or BRCA2 Mutation Carriers With Cancer Risk and Mortality. JAMA. 2010;304(9):967-975.
2. Hartmann LC, et al. Efficacy of bilateral prophylactic mastectomy in BRCA1 and BRCA2 gene mutation carriers. JNCI. 2001;93:1633-1637. 3. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast and Ovarian. v2.2017. Available at <http://www.nccn.org>.

Nipple Sparing Mastectomy with Reconstruction



Cleveland Clinic – courtesy of Dr. Risal Djohan

Rachel Cowden in the 21st Century



Ms. Cowden may not have died of breast cancer that young.

In conclusion:

**All women
deserve to
receive the
information
needed to allow
themselves to
make decisions
that they believe
are in their best
interest.**





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Every life deserves world class care.