

## Medical Hypothesis

# Pinch and quadrants: a mechanical hypothesis for the site-specific incidence of breast cancer

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**Abstract:** Breast cancer exhibits a well-documented but incompletely explained predilection for the upper outer quadrant (UOQ), accounting for 45-50% of all cases, followed by the lower inner quadrant (LIQ) as the second most common site. We propose a mechanical hypothesis: chronic, repetitive mechanical stress from sexual partner-initiated breast manipulation - specifically the four-finger pinch grasp - creates sustained micro-injury and subsequent reparative proliferation preferentially targeting the UOQ, thereby increasing local mutational burden. The thumb opposes on the LIQ, offering a natural explanation for its secondary incidence pattern. This hypothesis generates specific, testable predictions, including dose-response relationships between cumulative exposure and quadrant-specific risk, as well as lateral asymmetry based on partner handedness. A large-scale epidemiological questionnaire study is proposed as the initial validation step. If confirmed, this hypothesis may transform breast cancer risk reduction into a modifiable behavioral domain.

**Keywords:** Breast cancer, upper outer quadrant, mechanical stress, micro-injury, hypothesis, mechanotransduction

### Introduction

The anatomical distribution of breast cancer is non-random. Since the 1950s, clinical studies have consistently reported that the upper outer quadrant (UOQ) accounts for 45-50% of all breast malignancies, followed by the lower inner quadrant (LIQ) at approximately 15% [1-3]. This pattern has been replicated across diverse populations, suggesting a biological or physical determinant.

Existing explanations include greater glandular volume in the UOQ [4], and variations in vascular or lymphatic drainage [5]. However, none fully accounts for the consistent secondary peak in the LIQ. We propose an alternative explanatory framework based on extrinsic, repetitive mechanical loading from human sexual behavior.

### The hypothesis

#### Core proposition

Chronic, repetitive manual manipulation of the female breast by a sexual partner - specifically

the grasping and kneading action typical of human sexual behavior - imposes mechanical stress that causes subclinical micro-injury to breast epithelial and stromal tissues. Consequent cycles of injury, inflammation, and reparative proliferation increase local DNA replication errors and mutagenic risk. The biomechanics of the human hand predict a non-uniform distribution of this stress, corresponding to the observed cancer distribution.

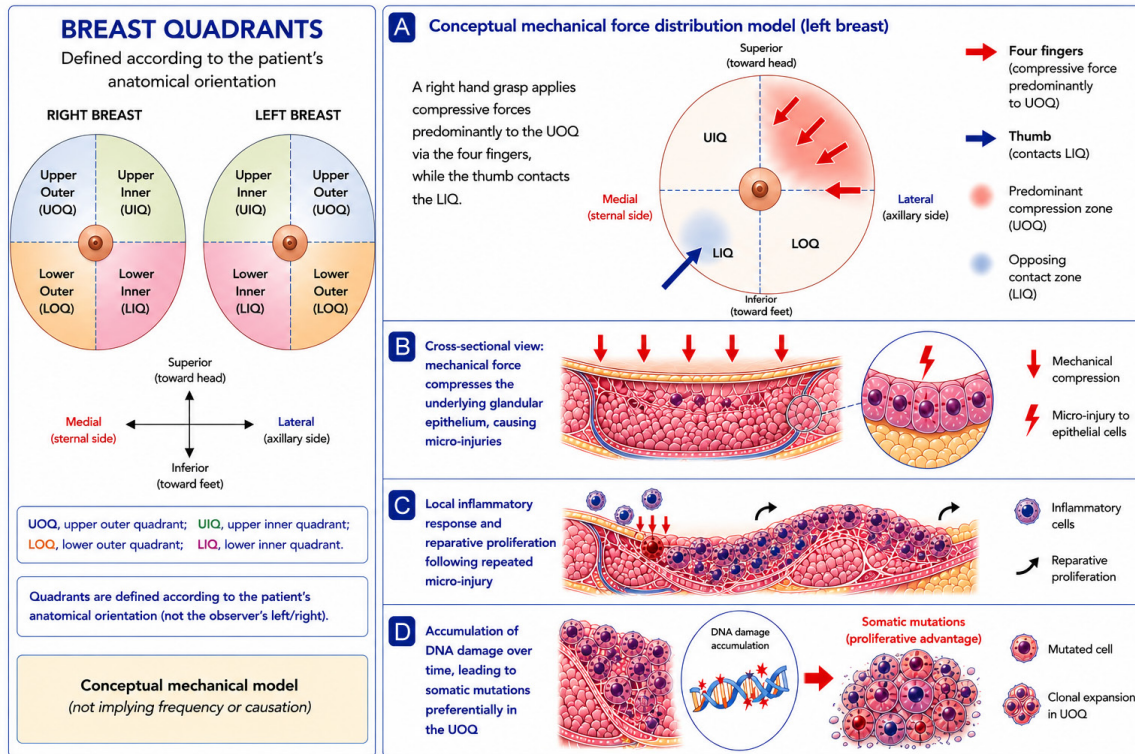
#### The biomechanical model of the grasp

When a partner manually manipulates a breast in a typical grasping motion:

- Four fingers (index, middle, ring, little) curl around the breast, applying compressive and shearing forces predominantly to the upper outer quadrant.
- The thumb opposes on the lower inner quadrant, balancing the digital pressure.

Thus, the hand functions as a mechanical stressor with intrinsic spatial asymmetry: the UOQ receives the highest cumulative pressure

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**Figure 1.** Hypothesized contribution of mechanical microtrauma to upper outer quadrant (UOQ) breast cancer. A. A right-handed grasp on the left breast. The four fingers apply compressive forces predominantly to the UOQ, while the opposing thumb contacts the LIQ. B. Cross-sectional view: mechanical force compresses the underlying glandular epithelium, causing micro-injuries. C. Local inflammatory response and reparative proliferation following repeated micro-injury. D. Accumulation of DNA damage over time, leading to somatic mutations preferentially in the UOQ. UOQ, upper outer quadrant; LIQ, lower inner quadrant.

(four fingers), the LIQ receives moderate pressure (thumb), and the remaining quadrants receive minimal contact (**Figure 1**).

This mechanical pattern mirrors the known cancer incidence rank order: UOQ (highest) > LIQ (second) > other quadrants (lower).

### Proposed mechanism

Repetitive mechanical stress is an established inducer of tissue micro-injury. Each grasping episode may cause basement membrane micro-disruptions, epithelial cell deformation, inflammatory infiltration, and recruitment of reparative proliferation. Each round of repair necessitates cell division. In the breast, which has low baseline mitotic activity, repeated injury-repair cycles artificially drive clonal expansion in a site-specific manner over years. The UOQ, as the primary stress recipient, undergoes the most frequent repair cycles, accumulating the highest mutational load. Mechanical

stress has been shown to induce DNA damage in other tissues: cyclic compression upregulates senescence-associated secretory phenotype in chondrocytes [6], and sustained pressure triggers double-strand breaks in epithelial cells [7].

We explicitly limit the scope of this hypothesis to female breast cancer in heterosexual partnerships. The mechanical principle may generalize, but the specific predictions are derived from this context.

### Evaluation of the hypothesis

#### Consistency with known biology

The hypothesis is grounded in established principles: (i) chronic inflammation increases cancer risk; (ii) repeated injury-repair cycles drive clonal expansion; (iii) mechanical force transduces via YAP/TAZ, Piezo channels, and integrin signaling pathways [8, 9].

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## *Addressing potential counterarguments*

Objection 1: The UOQ simply has more glandular tissue. Response: While the UOQ contains 35-40% of glandular volume, it accounts for 45-50% of cancers - a 10-15% excess. Our mechanical gradient explains both the excess and the LIQ's secondary position.

Objection 2: No animal model evidence. Response: No study has tested this. A straightforward rodent model (daily compression to one mammary gland vs. contralateral control) could directly test the hypothesis.

Objection 3: The topic is sensitive. Response: Large-scale sexual behavior surveys have been successfully conducted with appropriate ethical safeguards.

## **Empirical predictions**

As a hypothesis article, we present no experimental data. We offer a falsifiable framework for independent testing.

Prediction 1 (dose-response and site-specificity). Among women with at least one long-term sexual partnership (>2 years), cumulative mechanical exposure - quantified as frequency × average duration × intensity - will show a positive association with UOQ cancer risk, a weaker association with LIQ risk, and no association with LOQ (lower outer quadrant) risk as a negative control.

Prediction 2 (laterality asymmetry). Because a right-handed partner applies greater force with the dominant hand (typically on the partner's left breast), the left breast will show a higher proportion of UOQ cancers than the right breast. This lateral difference should be absent or reversed in left-handed couples.

Prediction 3 (effect modification by BMI). Women with lower body mass index (less adipose padding) will show a stronger exposure-risk association for a given reported manipulation intensity.

## **Proposed validation study**

We propose a multicenter case-control study using a structured questionnaire capturing partnership history, frequency/intensity of breast manipulation, hand posture, and stan-

dard reproductive confounders. The laterality discordant analysis within the same woman provides a quasi-experimental control for recall bias. This questionnaire can be added to ongoing cohort studies or administered in clinic settings at modest cost.

## **Consequences of the hypothesis**

If confirmed: Modifiable behavioral advice could lower risk without drugs or genetic screening. The quadrant distribution would be recognized as a processed outcome of life history. Mechanotransduction pathways in breast epithelium could become therapeutic targets.

If refuted: The search for the cause of quadrant-specific incidence continues, but our framework will have been tested and dismissed - equally valuable for scientific progress.

## **Conclusion**

The upper outer quadrant dominance in breast cancer has remained unexplained for over half a century. We propose that the human hand, in its ordinary sexual expression, may act as a mechanical risk factor: the four-finger grasp preferentially injures the UOQ, the thumb opposes on the LIQ, and the resulting gradient of cumulative micro-injury and repair generates the observed cancer topography. This hypothesis is specific, testable, and amenable to low-cost epidemiological verification. We invite independent research groups to test our predictions.

## **Disclosure of conflict of interest**

None.

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