

## Title: Solution proposed to a 2000-year-old problem in oncology

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### Abstract

A bimodal pattern of hazard of relapse among early stage breast cancer patients has been identified in multiple databases from US, Europe and Asia. We are studying these data to determine if this can lead to new ideas on how to prevent relapse in breast cancer. Using computer simulation and access to a very high-quality database from Milan for patients treated with mastectomy only, we proposed that relapses within 3 years of surgery are stimulated somehow by the surgical procedure. Most relapses in breast cancer are in this early category.

Retrospective data from a Brussels anesthesiology group suggests a plausible mechanism. Use of ketorolac, a common NSAID analgesic used in surgery was associated with far superior disease-free survival in the first 5 years after surgery. The expected prominent early relapse events in months 9-18 are reduced 5-fold. Transient systemic inflammation accompanying surgery (identified by IL-6 in serum) could facilitate angiogenesis of dormant micro metastases, proliferation of dormant single cells, and seeding of circulating cancer stem cells (perhaps in part released from bone marrow) resulting in early relapse and could have been effectively blocked by the perioperative anti-inflammatory agent. If this observation holds up to further scrutiny, it could mean that the simple use of this safe, inexpensive and effective anti-inflammatory agent at surgery might eliminate early relapses. We suggest this would be most effective for triple negative breast cancer and be especially valuable in low and middle-income countries. Similar bimodal patterns have been identified in other cancers suggesting a general effect. Based on the writings of Galen and Celsus, metastatic stimulation after surgery was known 2000 years ago.

writings of Galen and Celsus, such an effect was known to premodern physicians 2000 years ago.

### Recent Publications

1. Romano Demicheli and Michael W Retsky; A dormancy-based model for breast cancer: new findings and possible extension to other sites. *Breast Cancer Management, Future Medicine*. Vol. 3, No. 4 , Pages 311-314, 2014 (doi:10.2217/bmt.14.23) <http://www.futuremedicine.com/doi/abs/10.2217/bmt.14.23?journalCode=bmt>
2. MW Retsky; How long should adjuvant chemotherapy be given in early stage colon cancer? *Clinical and Experimental Pathology*. 3:1 2013. <http://www.omicsonline.org/2161-0681/2161-0681-3-136.digital/2161-0681-3-136.html>
3. Retsky M (2015) Colonoscopy to Prevent Colon Cancer: It Works but There Seems to be a Quality Issue. *J Cancer Sci Ther* 7: 292-293. doi:10.4172/1948-5956.1000365.
4. Perioperative Inflammation as Triggering Origin of Metastasis Development. M Retsky and R Demicheli editors. Springer-Nature 2017
5. Retsky M, Demicheli R. Multimodal Hazard Rate for Relapse in Breast Cancer: Quality of Data and Calibration of Computer Simulation. *Cancers (Basel)*. 2014 Nov 27;6(4):2343-2355. PubMed PMID: 25437254. <http://www.mdpi.com/2072-6694/6/4/2343>



### Biography

Michael Retsky (PhD in Physics from University of Chicago) made a career change to cancer research thirty years ago. He is Research Associate at Harvard TH Chan School of Public Health and Honorary Reader at University College London. He was on Judah Folkman's staff at Harvard Medical School for 12 years. Retsky is Editor of a Springer-Nature book on the breast cancer project published July 2017. After diagnosis of stage IIIc colon cancer in 1994, he was the first person to use what is now called metronomic adjuvant chemotherapy. He is a founder and for 10 years was on the Board of Directors of the Colon Cancer Alliance. He has published more than 70 papers in physics and cancer.

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