AUTOMATION OF THE ESTIMATION OF HUMAN OVARIAN RESERVE

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My Background

- Senior Research Fellow in Maths & Computer Science
  - University of St Andrews, Scotland
- Constrained optimisation & minimisation
  - Roger Fletcher was my MSc supervisor
- Casimir forces
  - similar to van der Waals forces - poorly understood, both in theory & practice
- Symmetry & search
  - where growth in both search space & number of symmetries is super-exponential

Medical/Biological Research

- Co-director of the Wallace Kelsey Research Foundation
  - www.wallacekelsey.org.uk
- We are interested in the late effects of cancer treatments on the survivors of childhood cancer
  - 70% - 80% of children with cancer survive
  - The radio- and chemotherapies also damage healthy cells
- In particular, we concentrate on the fertility of survivors

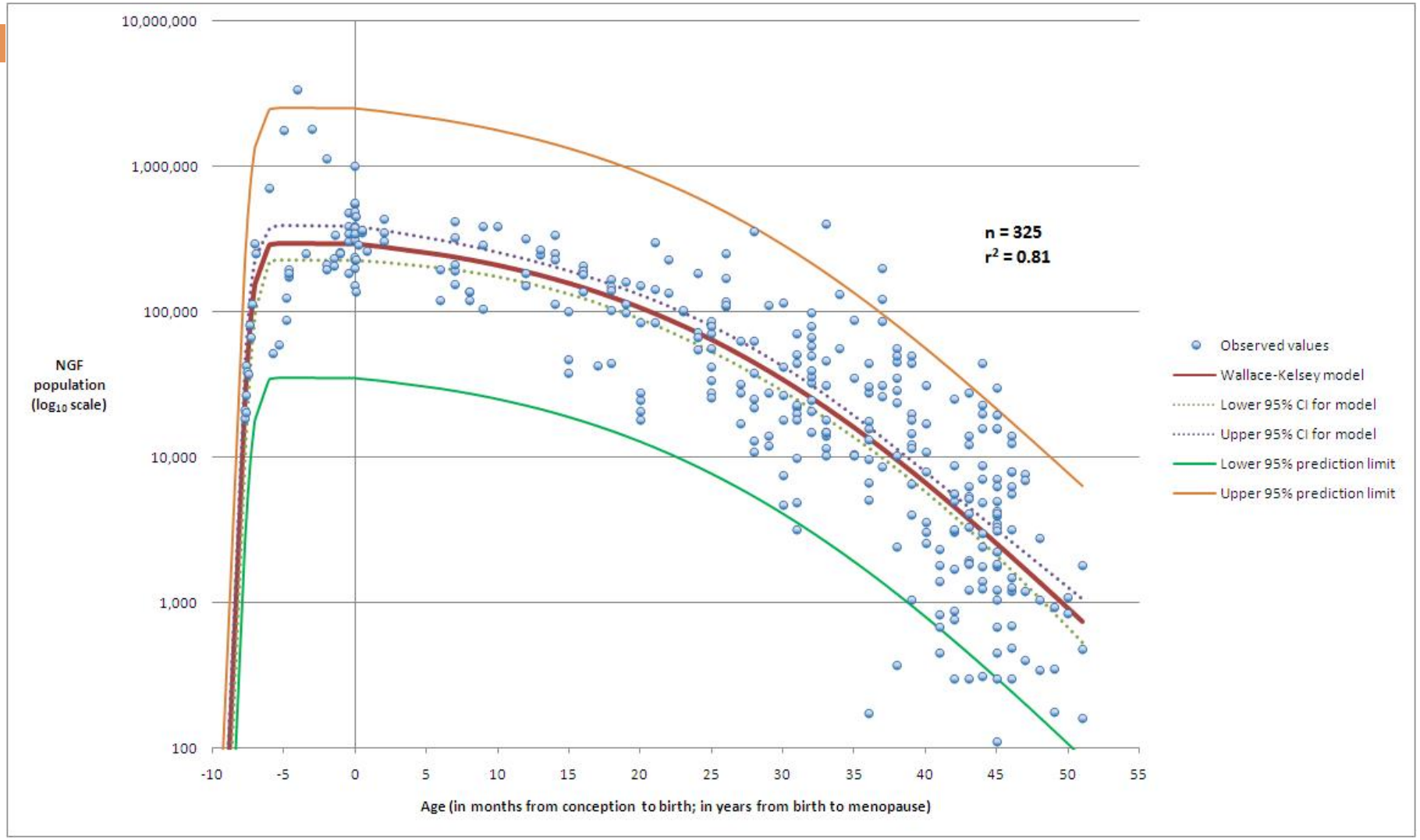
There are two questions

- Can we quantify the effects of radio- and chemotherapies in order to predict early menopause?
  - We published papers on this in 2004 & 2005
  - We are working with the US CCSS on new techniques based on new data and new models
- Can we predict age of menopause for healthy women?
  - Reproductive biologists have no good results
  - But we need this as our baseline calculation

Non-growing follicles (NGF)

- The human ovary contains a population of non-growing follicles
  - oocytes, ovocitos
- Some of these are recruited every 80-90 days
  - primary, secondary and antral follicles
  - most die off through atresia, but some become eggs
- When less than 1,000 remain, menopause occurs
  - so the population defines ovarian reserve in women
  - and the rate of decline is the “biological clock”

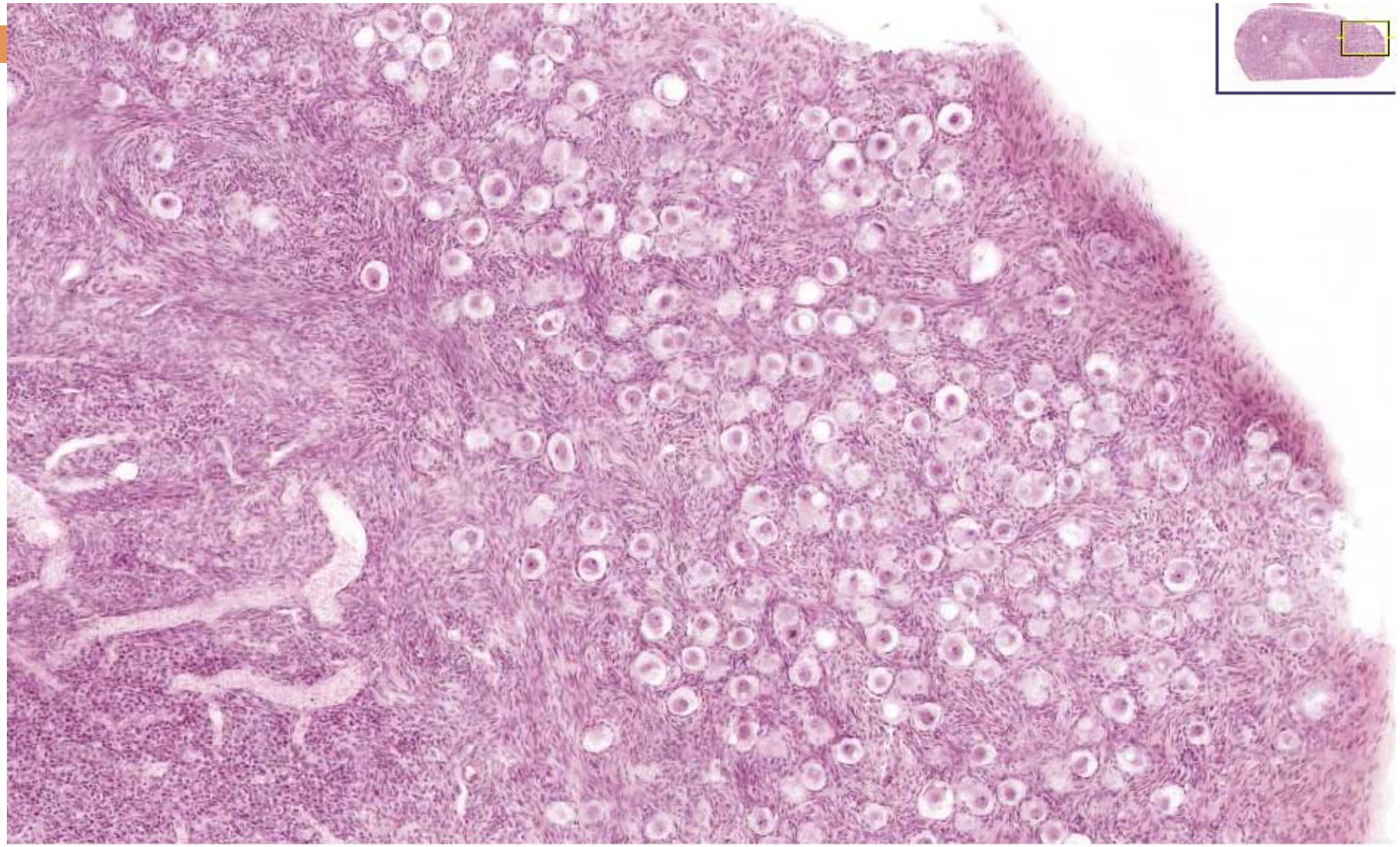
The Wallace-Kelsey Model



The Wallace-Kelsey Model

- Wallace WHB, Kelsey TW (2010) *Human Ovarian Reserve from Conception to the Menopause.*
  - PLoS ONE 5(1): e8772. doi:10.1371/journal.pone.0008772
  - The first model of ovarian reserve from conception
  - Agrees with separate studies on ages at menopause
- All the data was obtained by hand
  - Ovaries are sliced, stained & photographed
  - Sample population counts are integrated to get an estimate for the entire ovary

Ovarian tissue



Research in Uruguay

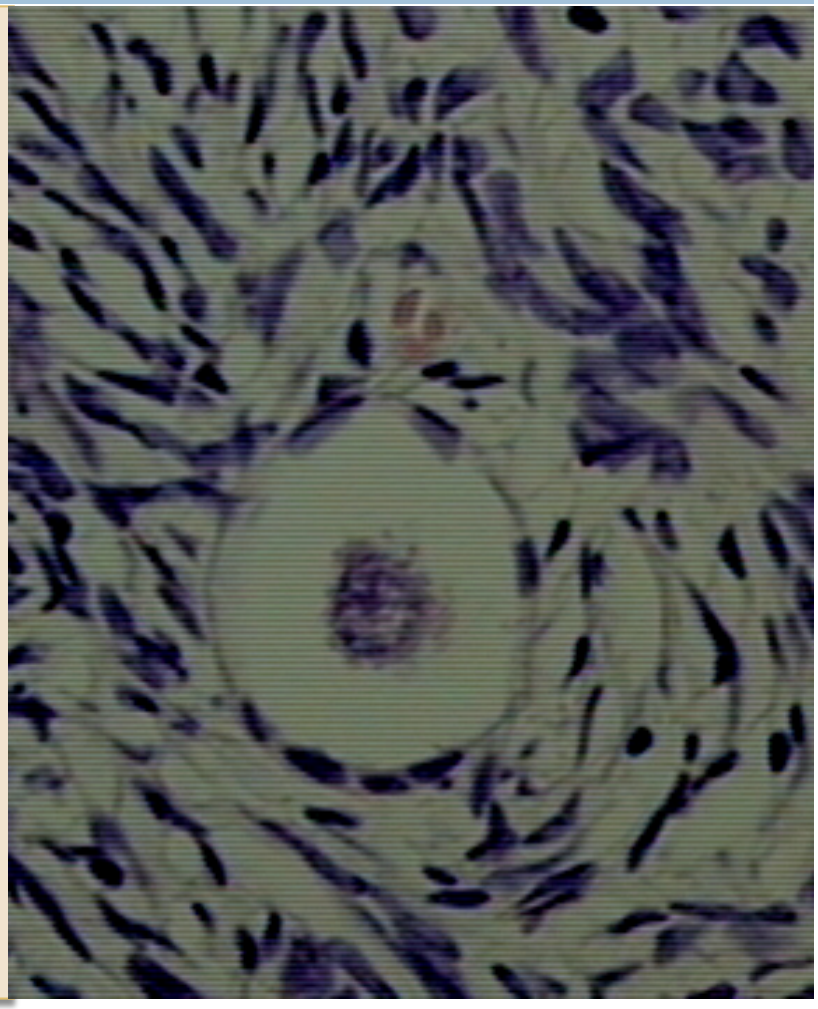
- Luis Castillo
  - Clinical Director, Fundacion Peluffo Giguens
  - Oncologist, also interested in late effects
- Pancho Coppola
  - Gynocologist at Perreira Rossell
- Benedicta Caserta
  - Histopathologist at Perreira Rossell
- We obtained ethical approval in 2008 for the study
  - I'm here to write up our results and submit to a journal

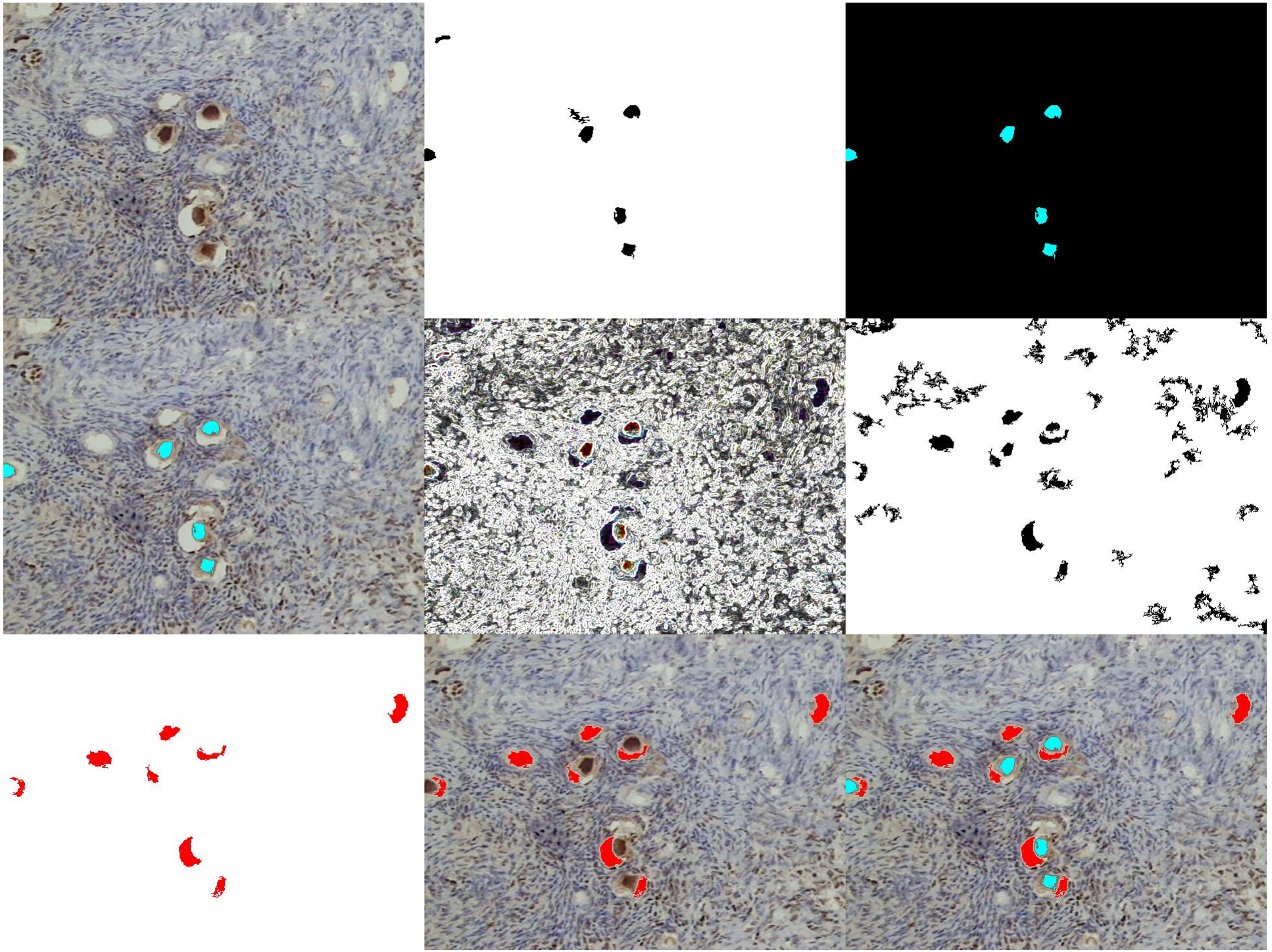
Research in Uruguay

- The idea is to automate the population counts
  - input photos to a system that automatically identifies and counts the follicles that define ovarian reserve
  - more accurate than humans
  - we can process more of the ovary
  - and hence reduce errors at the integration stage
- It should be possible to count all the follicles in an entire ovary
  - but that's the next study
  - if we get funding

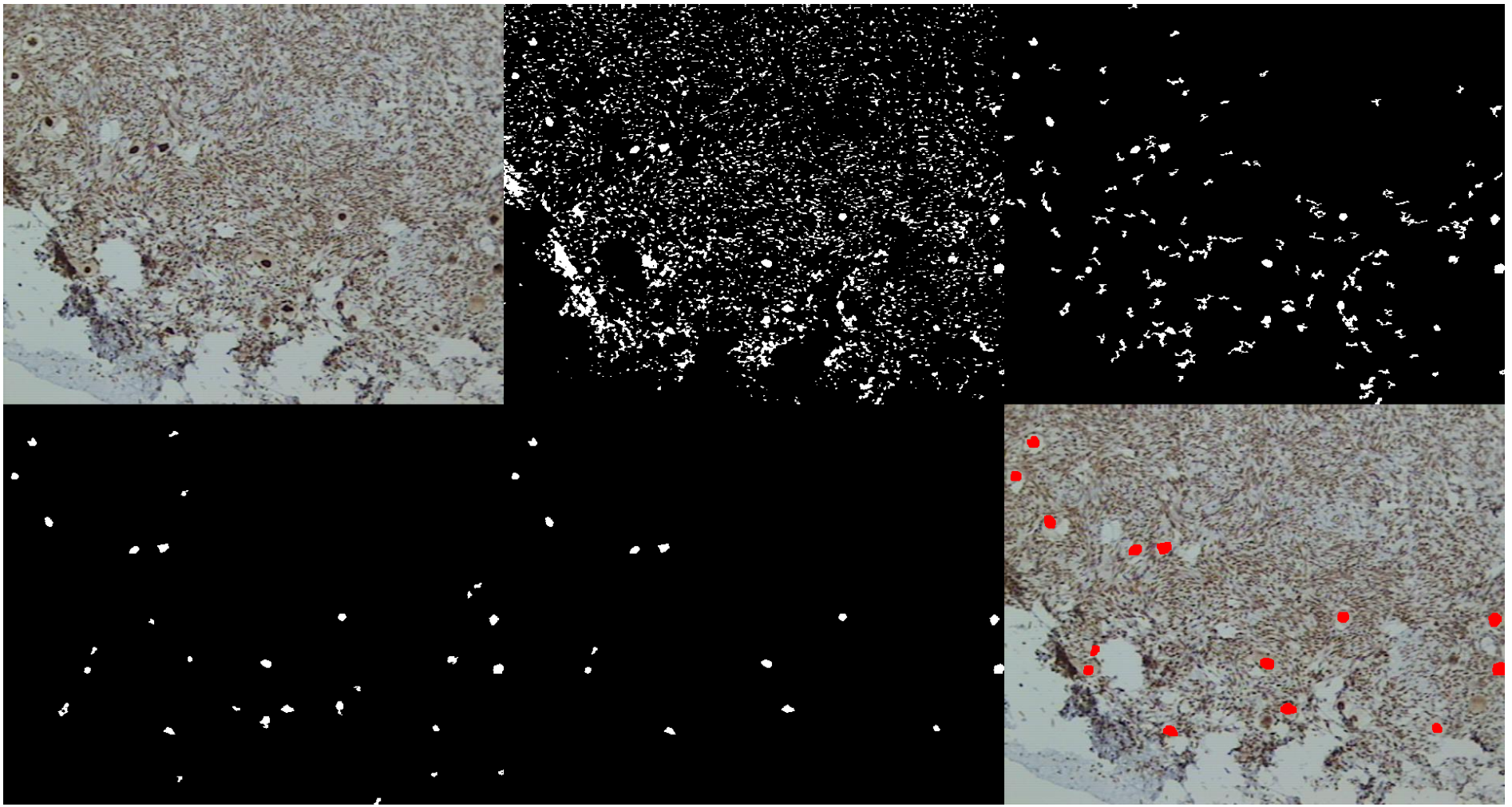
Research in Uruguay

- Counting follicles at high magnification is easy
  - but you need more photos and more lab time
- Our main advance is finding a stain that allows us to identify follicles at low magnification
  - H & E is the standard stain
  - We use PCNA

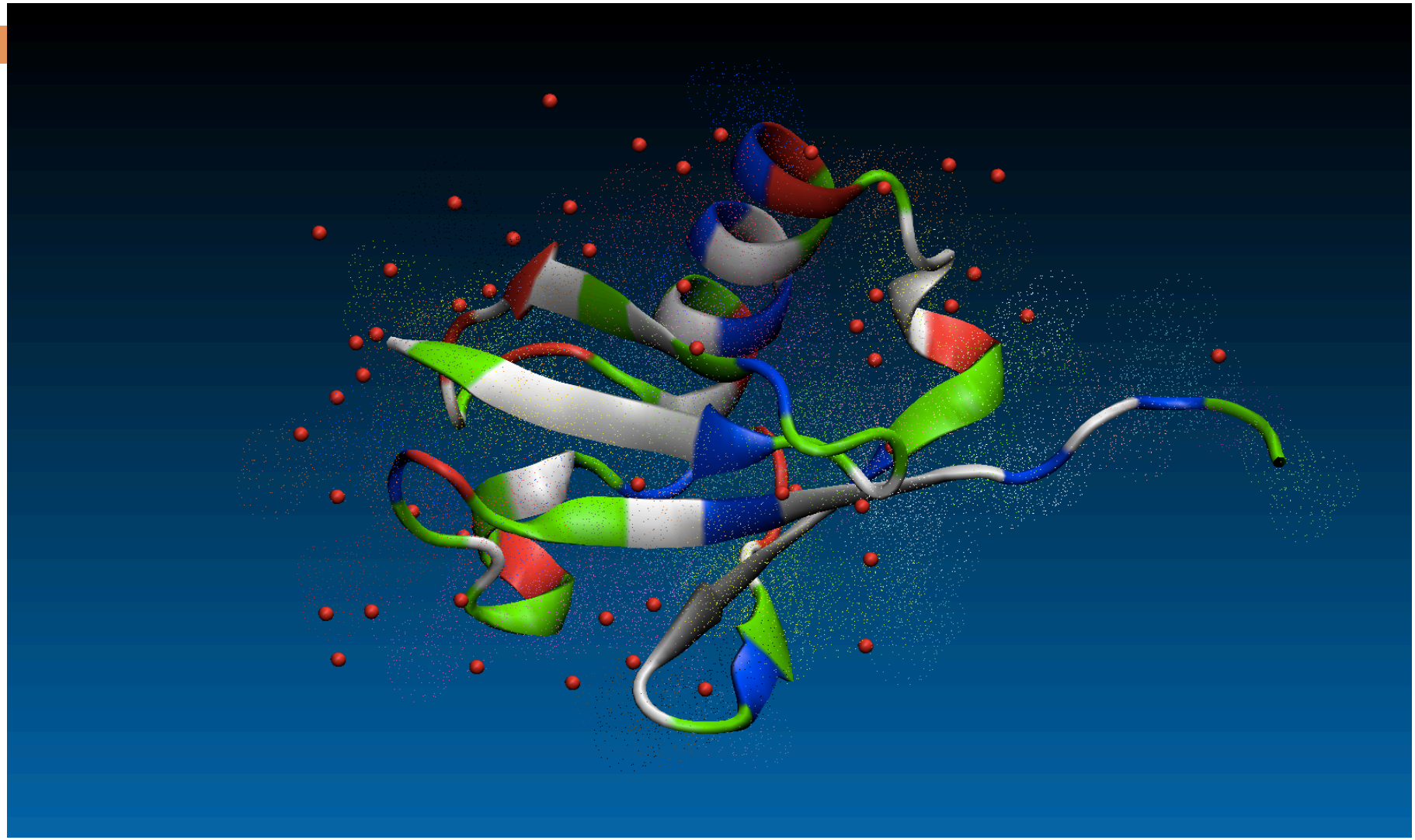




Good results even at 100x



Research in Uruguay

- We can tune the code to be conservative…
  - few false positives
- … or liberal
  - few false negatives
- The estimated true population is in the middle
- We still have some technical issues to resolve
  - what if we change the camera (or microscope, or technician)?
- But we will submit our paper for review in March

Muchas gracias, y he aprendido mucho