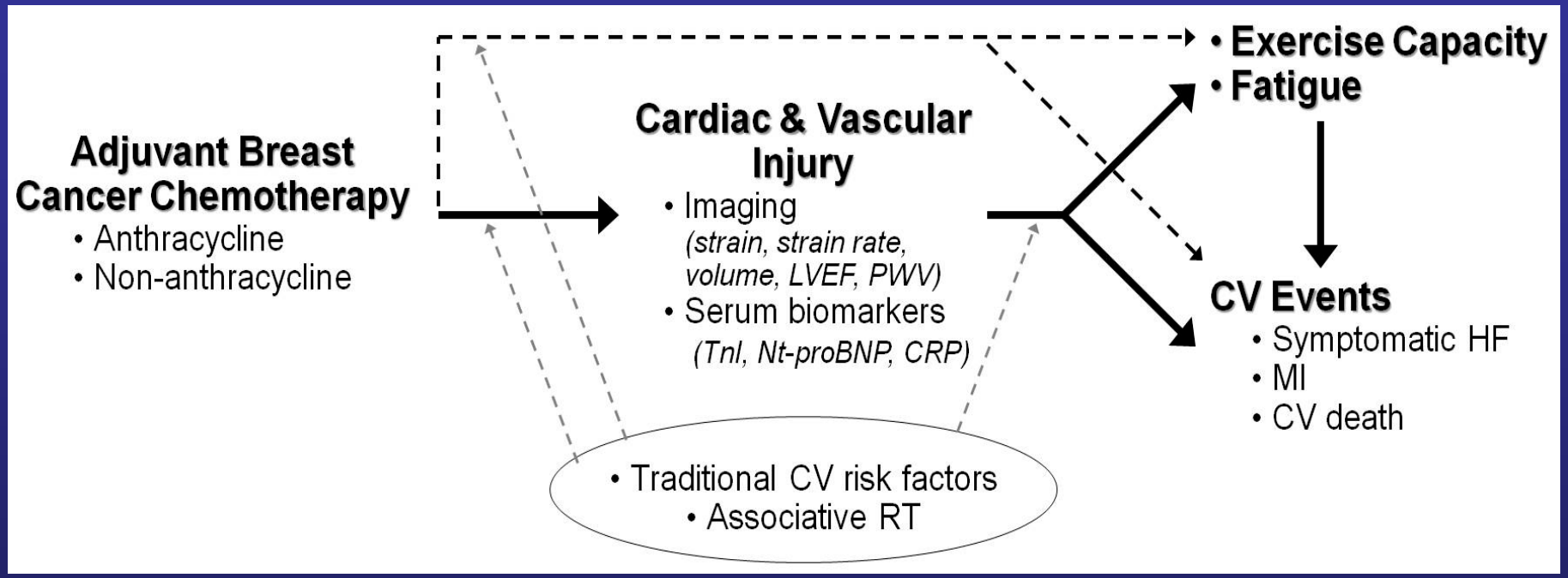
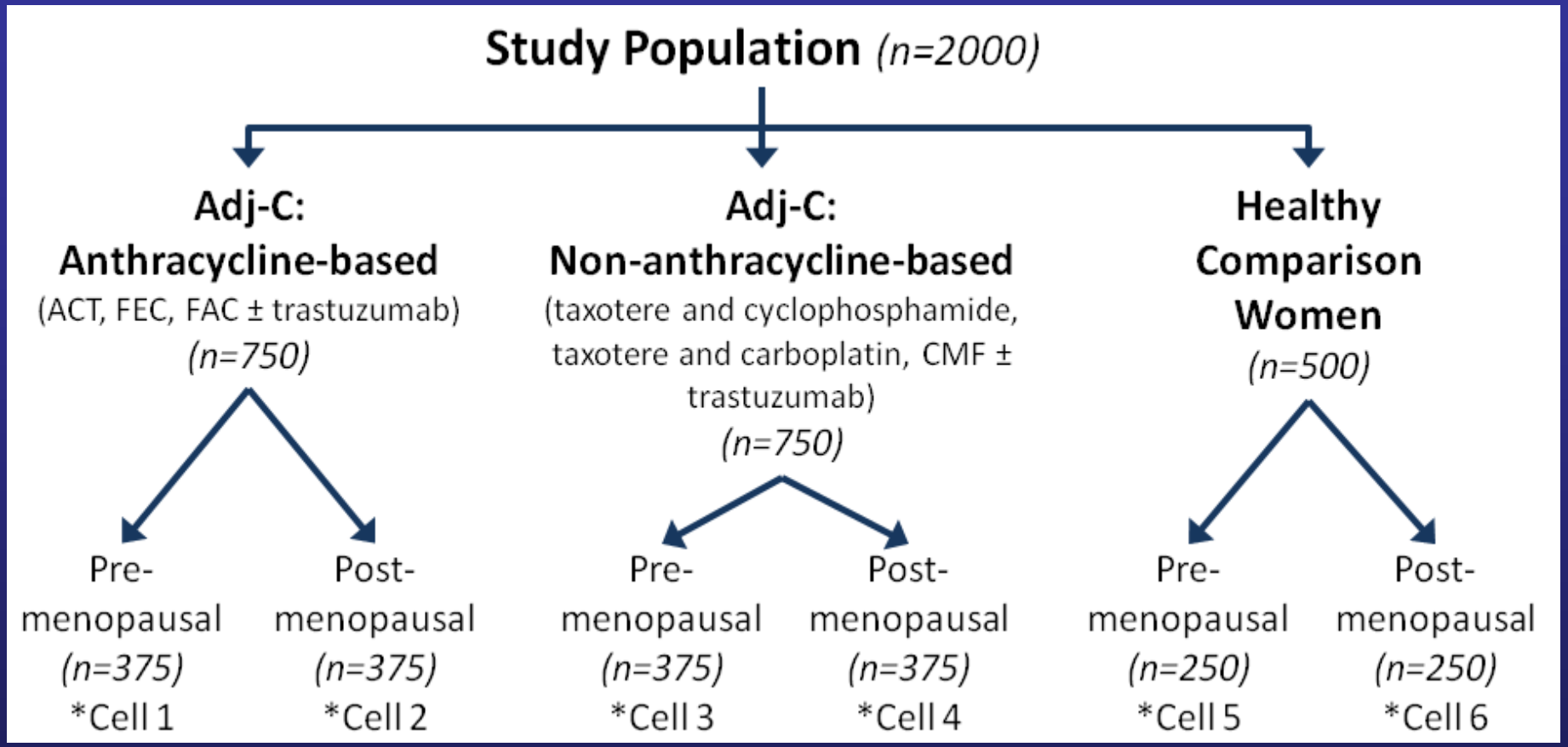
Conceptual Model



This study will address the relationships between cancer therapy, CV injury, exercise intolerance, fatigue, and CV events as primary outcomes. Relative contributions of age, menopause status, race/ethnicity, and radiation therapy (RT), as well as psychosocial and behavioral risk factors will be analyzed as covariates.

Recruitment Stratification



We will recruit 1,500 breast cancer patients receiving adjuvant chemotherapy – 750 receiving Anth and 750 receiving non-Anth – and 500 healthy comparison women. Recruitment will be stratified such that in each of these groups, 50% will be pre- and 50% post-menopausal, and 25% will be African-American (Cells 1-6).

Study Parameters and Time Course

Evaluation/Procedure	Baseline	Mo. 1	Mo. 3	Mo. 9	Mo. 12	Mo. 18	Mo. 24
Vitals (Heart rate, Blood pressure)	X		X	X			X
Demographics (Height, Weight, BMI, Waist circumference)	X		X	X			X
Evaluation of Menopausal Status	X						
Labs/Biomarkers							
Lipid panel, Serum Creatinine, CRP, Glucose, Hematocrit							
Adj-C Groups	X		X	X			X
Control Group	X		X				X
Labs/Biomarkers (All Groups)							
Nt-pro-BNP	X						X
Labs/Biomarkers							
Troponin							
Adj-C Groups	X	X	X	X			
Control Group	X		X				
DNA Storage (Adj-C Groups)	X						
MRI							
LVEDV, LVESV, LVSV, LVEF, LV strain Aortic wall thickness and PWV							
Adj-C Groups	X		X	X			X
Control Group	X		X				X
Exercise Testing							
6-minute walk	X		X	X	X	X	X
CPET (Peak VO_2, Exercise time)	X						X
Questionnaires							
Fatigue, Psychosocial/Behavioral Risk Factors, Sociodemographics, Comorbidities, Health-related Quality of Life	X		X	X	X	X	X
Outcomes Surveillance							
Continues q6mo for 10 yrs. after study initiation & 8 yrs. after enrolling each participant					X	X	X→

Assessments of New Patients Available for Enrollment

Site	Eligible Women Per Year (Stage I-III, presenting for adjuvant chemotherapy)	Expected annual enrollment (1 in 6)	Expected Total enrollment (over 2.5 years)	Expected # of women eligible based on site demographics*				
				Race/Ethnicity			Menopausal Status	
				Caucasian	African-American	Hispanic	Pre-menopause	Post-menopause
Wake Forest CCOP	186	31	78	60	15	2	26	52
Forsyth CCOP	144	24	60	52	6	1	20	40
Charlotte Presbyterian CCOP	160	27	67	45	19	2	26	41
Greenville CCOP	478	80	199	159	30	6	44	155
Upstate Carolina CCOP	300	50	125	88	26	8	28	98
Wichita CCOP	312	52	130	70	25	26	47	83
Northwestern	792	132	330	238	79	7	89	241
University of Alabama-Birmingham	540	90	225	185	36	2	101	124
UNC-Chapel Hill	482	80	201	149	42	6	60	141
University of Miami	395	66	165	41	41	82	49	115
UT-Southwestern	298	50	124	87	30	17	61	63
Total:	**4,087**	**681**	**1,703**	**1,174**	**349**	**158**	**550**	**1,153**
Target Enrollment (Adj-C groups):			**1,500**	**1,086**	**375**	**140**	**750**	**750**

Totals for eligible overall cancer cohort enrollment in each race/ethnicity and menopausal status category are shown. For clarity, our target

Committee Structure

Roman = Study Co-Investigators **Bold = Wake Forest Research Base** *Italic = Recruitment Sites*

*** Indicates committee chair**

Executive Committee
*Hundley
Burke
D'Agostino
Lash
Lawrence
Shaw

Steering Committee

*Hundley	Mihalko	*Rotating members*
Burke	Avis	*(sites)*
D'Agostino	Brubaker	*Hu (Miami)*
Kitzman	Brown	*Andrews (UT)*
Lash	Muss	*Lee (Northwestern)*
Lawrence	**Shaw**	*Ntim (Charlotte)*

Imaging
* Hundley
Vasu
Ge
Hamilton
Lee (NW)
Lloyd (UAB)
Ntim (Charlotte)

Safety/ DSMB
CROC
(*D'Agostino)
DSMB

Operations
* Hundley
Lash
Mihalko
Lane
Keith

Adjudication of CV Events
*Kitzman
Hundley
Burke

Recruitment/ Retention
*Mihalko
Lawrence
Hundley
Lane
*** Beech**
Enevold
Hu (Miami)

Ancillary Studies/ P&P
*Burke
D'Agostino
Lash
Lesser
Andrews (UT)

Exercise Testing:
* Kitzman
* Brubaker
Mihalko

Quality Control/ Database Management:
*Lash
Brubaker
Lawrence

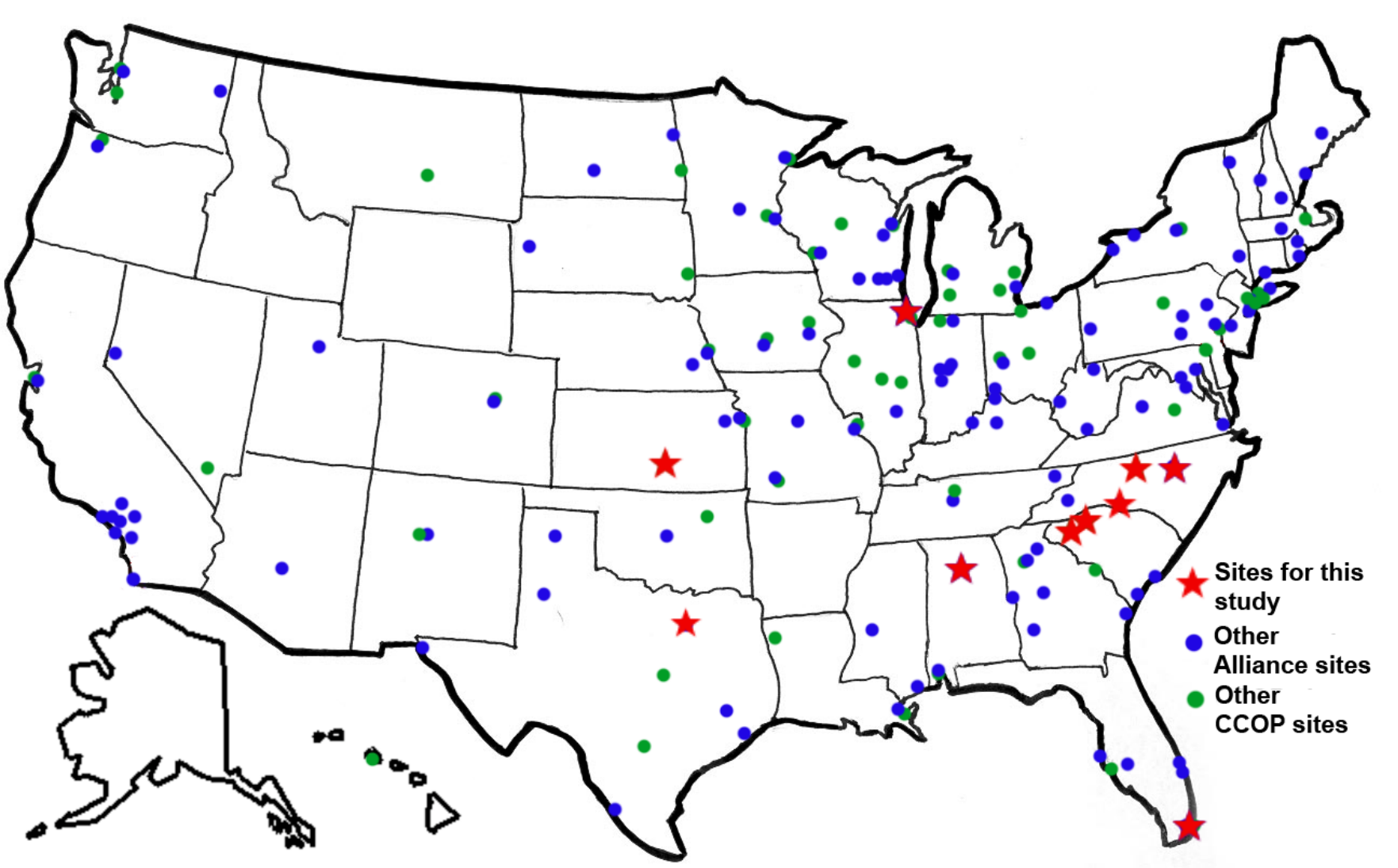
Behavioral Science:
*Avis
Mihalko
Rosdhal

Labs:
*Lawrence
Lane
Keith
Rosdhal
Yates

Radiation:
*Brown
Lawrence
Keith
Data Manager

Statistical Analysis:
*D'Agostino
Lash
Tan
2 Masters Level statisticians
1 Senior statistician

Map of CCOP and Alliance Sites



Targeted/Planned Enrollment

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino	186	0	186
Not Hispanic or Latino	1814	0	1814
Ethnic Category: Total of All Subjects *	2000	0	2000
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	52	0	52
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	500	0	500
White	1448	0	1448
Racial Categories: Total of All Subjects *	2000	0	2000

Exclusion Criteria

- LVEF<50%
- Uncontrolled hypertension
- Recent history of alcohol or drug abuse
- Inflammatory conditions
- Use of immunosuppressant agents
- Medical conditions that might compromise the safety or success of the study
- Intracranial metal or implanted devices
- Unstable angina
- Inability to exercise on treadmill or stationary cycle
- Significant ventricular arrhythmias
- Atrial fibrillation with uncontrolled ventricular response
- Acute myocardial infarction within 28 days
- Claustrophobia
- Pregnancy
- Those unable to provide informed consent or planning to move with 24 months of enrollment