Analysis of calcification in cadaveric carotid arteries and intracranial vasculature by three-dimensional visualization and histologic examination

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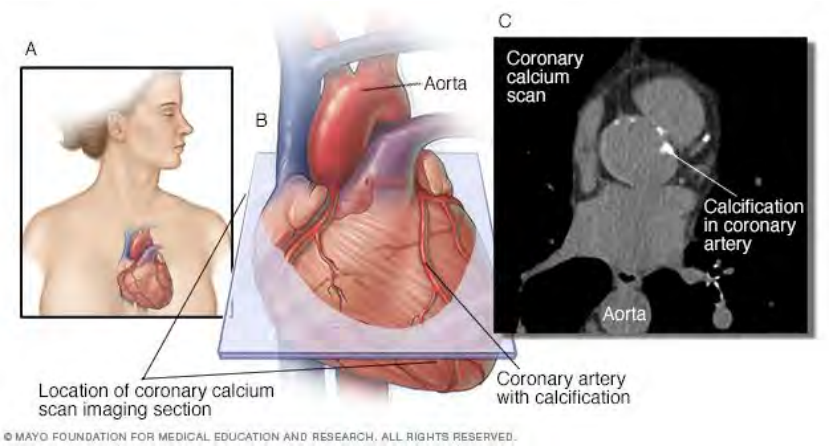
INTRODUCTION

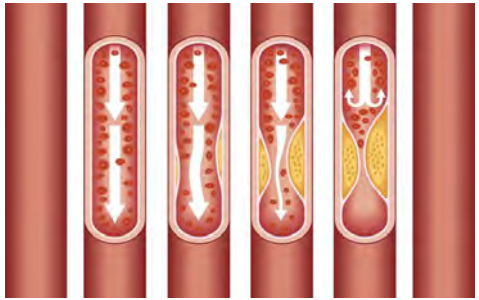
- **What is vascular calcification (VC)?**
  - VC occurs when calcium deposits in vascular tissue, leading to increased stiffness, loss of elasticity, and decreased compliance.
  - VC is a cardiovascular disease risk factor that is associated with increased morbidity and mortality in the general population. It has also been shown to accelerate coronary atherosclerosis.

- **What are the current clinical assessments of VC?**
  - X-rays, CT, Ultrasound
  - Electron beam CT
  - Coronary Artery Calcium Score (CACS)



INTRODUCTION

- **Who does VC affect?**
  - VC is prevalent in the elderly population, especially in the context of arteriosclerosis.
  - VC also affects individuals who may be at risk for cardiovascular events, chronic kidney disease, diabetes, and even some genetic disorders.
- **Why is VC potentially concerning?**
  - The presence and degree of calcification can predict the risk of mortality.
  - One study showed that the presence of calcification in any arterial wall was associated with a 3-4-fold increased risk in mortality and cardiovascular events.
  - Can helpful in patients with subclinical atherosclerosis to prevent further development of disease.



BACKGROUND

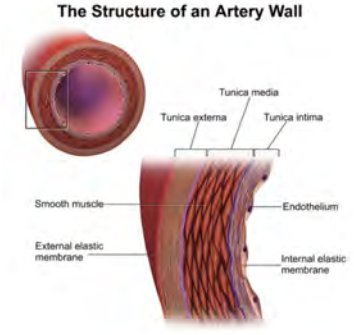
- Larger calcification load in the carotid arteries correlates with presence of cerebral infarcts and small vessel disease (Bos et al, 2011; Chen YC et al, 2019)

- Out of 31 human cadavers, mild-to-moderate calcification was found in 90% of the ECAs within the tunica media. Moderate-to-severe was found in the tunica media of 35% of the CCAs.

- Histopathologists still lack a standardized vascular calcification severity grading scale

- Goal is to promote a standardized calcification grading scale, based on one previously validated in coronary arteries (Nakamura et al, 2009)

Grade 0 - No calcification
Grade 1 - Calcification in **<25%** of cross-sectional area
Grade 2 - Calcification in **25-50%** of cross-sectional area
Grade 3 - Calcification in **51-75%** of cross-sectional area
Grade 4 - Calcification in **>75%** of cross-sectional area



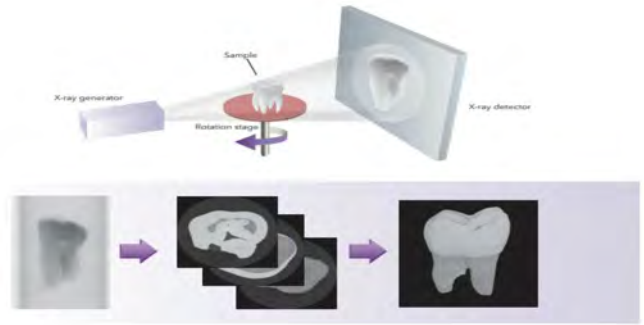
Blausen.com staff (2014). 'Medical gallery of Blausen Medical 2014'. WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436.

RATIONALE

- Given our understanding of the detrimental effects of VC in the periphery (i.e. its contribution to CVD), investigation of VC in the brain is warranted to examine its potential contribution to cerebrovascular disease. Given that EC carotid US is a clinically utilized measurement of stenosis, our study aims to examine the relationship between EC carotid calcification & IC VC

- This study is utilizing the CCAs and Circle of Willis from each cadaver

- Utilization of MicroCT will allow for more detailed examination of calcification within the vascular tissue

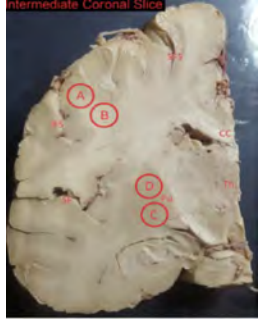


Micro Photonics. (2022, March 14). Retrieved April 22, 2022, from https://www.microphotonics.com/what-is-micro-ct-an-introduction/#:~:text=micro%2DCT%20scanners.-,What%20is%20the%20difference%20between%20medical%20CT%20and%20micro%2DCT,scale%20with%20greatly%20increased%20resolution.

HYPOTHESIS

- Trail blazing study that will examine the relationship between the Internal carotids and cerebral arterial microvasculature using a microCT
- We anticipate that the presence of calcification in an Internal carotid artery will correlate with calcification in the ipsilateral cerebral vasculature
- In addition we anticipate that if high amounts of Internal carotid calcification are present then the ipsilateral cerebral arteries will have a decreased volume

METHODS



- **What we've done so far:**
  - Collected Internal carotid arteries, cerebral arteries(ACA, MCA, PCA) and brain parenchymal(hippocampal and basal ganglia) samples from 30 cadavers which were stored in phosphate buffered solution with azide prior and perfused with MICROFIL
- **Next steps:**
  - Imaging with microCT(high resolution, Dragonfly and NRecon)
  - Categorizing calcification in relation to size, location and presence or absence of lipid pools
  - Samples will be histologically analyzed and graded for presence and location of calcification

LIMITATIONS

- No **medical history/clinical information** on cadavers

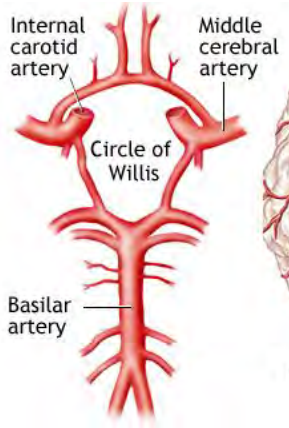
1) No cause of death
2) No knowledge of medical complications/conditions

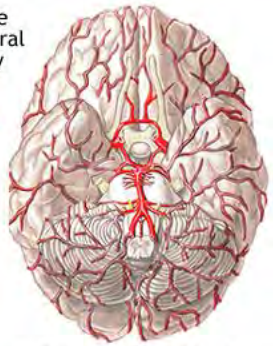
- *Inability* to image full brain

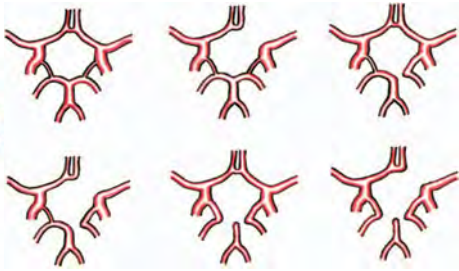
1) MicroCT limiting tissue sampling due to use of 50 mL vials → high resolution imaging

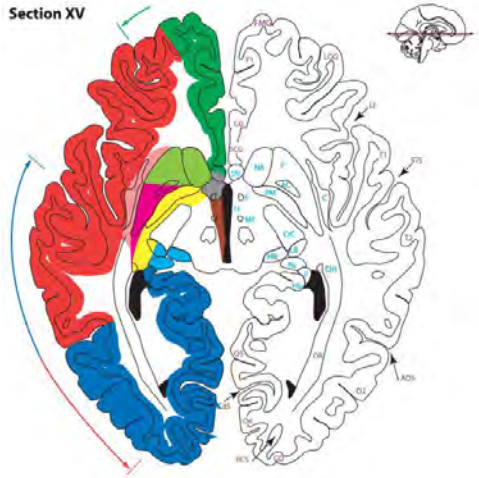
- Variability in vascular structures

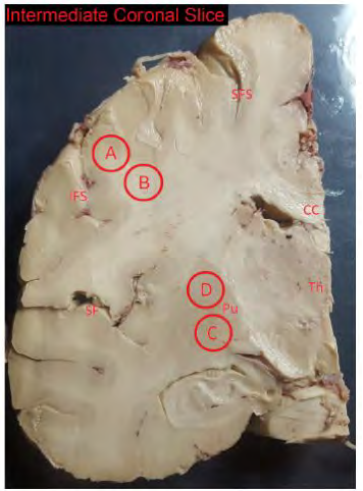
1) Difficult to decipher where one structure ends & another begins
2) Omission of structures due to variations in individuals' anatomy
3) Variability in anatomic location of parenchymal regions of interest











IMPLICATIONS

- **<u>Supported hypothesis:</u>** Intracranial arterial calcification plays potential key role in pathophysiology of ischemic stroke, cognitive deficit, and dementia
  - Shows (+) relationship between **external carotid calcification** & **internal carotid Circle of Willis** microvasculature
  - Future studies needed to investigate relationship between ICA VC & clinical features of cognitive decline, cerebrovascular disease, and vascular dementia

- **<u>Benefits of the study:</u>** Data will be valuable for designing future studies
  - i.e. refining methods for studying VC by comparing imaging data from cadavers to imaging data on living subjects)

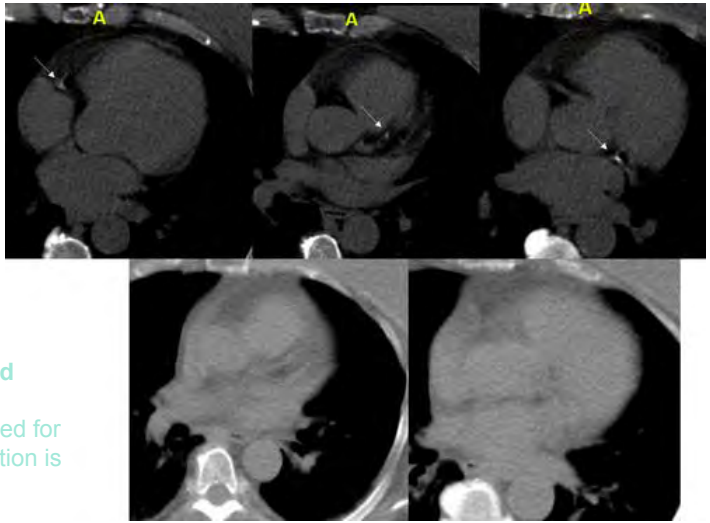


Figure. Images from a computed tomographic (CT) coronary artery calcium scan (top) of a 63-y-old woman (body mass index, 40) demonstrating mild calcification in each of the 3 coronary arteries (arrows) with an Agatston score of 121 AU. The blurred images of the 20 kv, nongated CT scan obtained for attenuation correction for a myocardial perfusion imaging study (**bottom**) are such that coronary calcification is not seen.

IMPLICATIONS

Table 3. Risk of Coronary Events Associated with Increasing Coronary-Artery Calcium Score after Adjustment for Standard Risk Factors.*

Coronary-Artery Calcium Score	Major Coronary Event†			Any Coronary Event		
	No./No. at Risk	Hazard Ratio (95% CI)	P Value	No./No. at Risk	Hazard Ratio (95% CI)	P Value
0	8/3409	1.00		15/3409	1.00	
1–100	25/1728	3.89 (1.72–8.79)	<0.001	39/1728	3.61 (1.96–6.65)	<0.001
101–300	24/752	7.08 (3.05–16.47)	<0.001	41/752	7.73 (4.13–14.47)	<0.001
>300	32/833	6.84 (2.93–15.99)	<0.001	67/833	9.67 (5.20–17.98)	<0.001
$Log_2(CAC+1)$‡		1.20 (1.12–1.29)	<0.001		1.26 (1.19–1.33)	<0.001

* CAC denotes coronary-artery calcium score, and CI confidence interval.
† Major coronary events were myocardial infarction and death from coronary heart disease.
‡ Each unit increase in $log_2(CAC+1)$ represents a doubling of the coronary-artery calcium score.

Table 4. Risk of Coronary Heart Disease Associated with Coronary-Artery Calcium Score in Four Racial or Ethnic Groups.

Thank you! Questions?

For additional questions/correspondence, email: **kborges@nyit.edu**

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