REFERENCES

[1] W. Anne and G. Allison, *Ross and Wilson Anatomy and Physiology in Health and Illness*, 11th ed. Edinburgh; New York: Churchill Livingstone, 2010.

[2] A. Shaw, B. Smith, and D. C. Howlett, "Axial CTA of the heart," in *FRCR Part 1 Anatomy Mock Examinations*, Cambridge University Press, 2011, p. 61.

[3] W. F. Boron and E. L. Boulpaep, "The heart," in *Medical Physiology, 2e Updated Edition: with Sudent Consult Online Access*, Elsevier Health Sciences, 2012, p. 581.

[4] J. T. Dodge, B. G. Brown, E. L. Bolson, and H. T. Dodge, "Intrathoracic spatial location of specified coronary segments on the normal human heart. Applications in quantitative arteriography, assessment of regional risk and contraction, and anatomic display," *Circulation*, vol. 78, no. 5 Pt 1, pp. 1167–1180, Nov. 1988.

[5] D. S. Baim, *Grossman's Cardiac Catheterization, Angiography, and Intervention*. Lippincott Williams & Wilkins, 2006.

[6] R. J. Myerburg and M. J. Junttila, "Sudden cardiac death caused by coronary heart disease," *Circulation*, vol. 125, no. 8, pp. 1043–1052, Feb. 2012.

[7] W. H. Organization, "Causes of death," in *The Global Burden of Disease: 2004 Update*, World Health Organization, 2008, pp. 7–26.

[8] Y. Yang, "Image segmentation and shape analysis of blood vessels with applications to coronary atherosclerosis," Georgia Institute of Technology, Atlanta, Georgia, 2007.

[9] R. Blankstein, "Introduction to noninvasive cardiac imaging," *Circulation*, vol. 125, no. 3, pp. e267–e271, Jan. 2012.

[10] "Stress echocardiography: MedlinePlus Medical Encyclopedia." [Online]. Available: https://www.nlm.nih.gov/medlineplus/ency/article/007150.htm. [Accessed: 14-Feb-2016].

[11] R. Mastouri, S. G. Sawada, and J. Mahenthiran, "Current noninvasive imaging techniques for detection of coronary artery disease," *Expert Rev. Cardiovasc. Ther.*, vol. 8, no. 1, pp. 77–91, 2010.

[12] R. Cardona and G. Gunabushanam, "Myocardial perfusion SPECT: background, indications, contraindications," *MedScape*, Jul. 2014.

[13] "Single Photon Emission Computed Tomography (SPECT)." [Online]. Available: http://www.heart.org/HEARTORG/Conditions/HeartAttack/SymptomsDiagnosisofHeartAttack/Single-Photon-Emission-Computed-Tomography-SPECT_UCM_446358_Article.jsp#.Vr_-f7R951s. [Accessed: 14-Feb-2016].

[14] N. R. Mollet, F. Cademartiri, and P. J. de Feyter, "Non-invasive multislice CT coronary imaging," *Heart*, vol. 91, no. 3, pp. 401–407, Mar. 2005.

[15] G. S. Wagner, O. Pahlm, and N. Kjell C., "Coronary angiography," in *Multimodal Cardiovascular Imaging: Principles and Clinical Applications*, 1st ed., McGraw-Hill Medical, 2011, pp. 71–80.

[16] "Intravascular ultrasound : MedlinePlus Medical Encyclopedia." [Online]. Available: https://www.nlm.nih.gov/medlineplus/ency/article/007266.htm. [Accessed: 17-Feb-2016].

[17] S. Bangalore and D. L. Bhatt, "Coronary intravascular ultrasound," *Circulation*, vol. 127, no. 25, pp. e868–e874, Jun. 2013.

[18] S. E. Nissen and P. Yock, "Intravascular ultrasound novel pathophysiological insights and current clinical applications," *Circulation*, vol. 103, no. 4, pp. 604–616, Jan. 2001.

[19] E. Grube, U. Gerckens, L. Buellesfeld, and P. J. Fitzgerald, "Intracoronary imaging with optical coherence tomography a new high-resolution technology providing striking visualization in the coronary artery," *Circulation*, vol. 106, no. 18, pp. 2409–2410, Oct. 2002.

[20] M. Terashima, H. Kaneda, and T. Suzuki, "The role of optical coherence tomography in coronary intervention," *Korean J. Intern. Med.*, vol. 27, no. 1, pp. 1–12, Mar. 2012.

[21] E. Jahangir and J. A. McPherson, "Fractional Flow Reserve Measurement: Background, Indications, Outcomes," *Medscape*, Dec. 2015.

[22] P. Vranckx, D. E. Cutlip, E. P. McFadden, M. J. Kern, R. Mehran, and O. Muller, "Coronary pressure–derived fractional flow reserve measurements recommendations for standardization, recording, and reporting as a core laboratory technique. proposals for integration in clinical trials," *Circ. Cardiovasc. Interv.*, vol. 5, no. 2, pp. 312–317, Apr. 2012.

[23] P. A. L. Tonino *et al.*, "Angiographic versus functional severity of coronary artery stenoses in the FAME study Fractional Flow Reserve Versus Angiography in multivessel evaluation," *J. Am. Coll. Cardiol.*, vol. 55, no. 25, pp. 2816–2821, Jun. 2010.

[24] "Angioplasty and stent placement for the heart." [Online]. Available: http://www.hopkinsmedicine.org/healthlibrary/test_procedures/cardiovascular/angioplasty_and_stent_placement_for_the_heart_92,p07981/. [Accessed: 02-Dec-2016].

[25] M. T. Dehkordi, S. Sadri, and A. Doosthoseini, "A review of coronary vessel segmentation algorithms," *J. Med. Signals Sens.*, vol. 1, no. 1, pp. 49–54, 2011.

[26] C.-Y. Lin and Y.-T. Ching, "Extraction of Coronary Arterial Tree using cine X-ray angiograms," *Biomed. Eng. Appl. Basis Commun.*, vol. 17, no. 03, pp. 111–120, Jun. 2005.

[27] A. Takagi, Y. Tsurumi, N. Magosaki, K. Suzuki, K. Nakamura, and H. Kasanuki, "Significance of angiographic haziness at the distal stent edge: analysis by intravascular ultrasound and quantitative coronary angiography," *J. Cardiol.*, vol. 33, no. 6, pp. 307–316, Jun. 1999.

[28] M. Wang, C. Li, W. Cai, and X. Wu, “Coronary angiography image edge detection based on information measure,” in *2010 WASE International Conference on Information Engineering (ICIE)*, 2010, vol. 1, pp. 141 –144.

[29] M. S. D. Kumar, D. Shen, L. Wei, R. Turlapthi, and J. S. Suri, “Motion correction strategies for interventional angiography images: a comparative approach,” in *IEEE International Conference on Image Processing, 2007. ICIP 2007*, 2007, vol. 1, pp. I –497 –I –500.

[30] M. Schrijver, “Angiographic image analysis to assess the severity of coronary stenoses,” info:eu-repo/semantics/doctoralThesis, Universiteit Twente, Enschede, 2002.

[31] K. Sun, S. Jiang, and Y. Wang, “Segmentation of coronary artery on angiogram by combined morphological operations and watershed,” in *2nd International Conference on Biomedical Engineering and Informatics, 2009. BMEI ’09*, 2009, pp. 1–4.

[32] K. Thayalan, “Fluoroscopy imaging,” in *The Physics of Radiology and Imaging*, 1st ed., New Delhi, India ; Philadelphia: Jaypee Brothers Medical Pub, 2014, pp. 205–241.

[33] “Medical X-ray imaging - fluoroscopy.” [Online]. Available: http://www.fda.gov/Radiation-EmittingProducts/RadiationEmittingProductsandProcedures/MedicalImaging/MedicalX-Rays/ucm115354.htm. [Accessed: 04-Mar-2016].

[34] Mosby, *Mosby’s Pocket Dictionary of Medicine, Nursing & Health Professions*. Elsevier Health Sciences, 2009.

[35] “View details of Philips Allura Xper FD10.” [Online]. Available: http://www.usa.philips.com/healthcare/product/HC722022CA/allura-xper-fd10-xray-system. [Accessed: 02-Dec-2016].

[36] E. L. Nickoloff, "AAPM/RSNA physics tutorial for residents: Physics of flat-panel fluoroscopy systems," *RadioGraphics*, vol. 31, no. 2, pp. 591–602, Mar. 2011.

[37] M. S. V. Lysel, "X-Ray projection angiography," in *The Biomedical Engineering Handbook 1*, 2nd ed., Springer Science & Business Media, 2000, pp. 61.8 – 61.18.

[38] "The image intensifier." [Online]. Available: http://www.upstate.edu/radiology/education/rsna/fluoro/iisize.php. [Accessed: 02-Dec-2016].

[39] Q. B. Carroll, "Image intensification device," in *Practical Radiographic Imaging*, 8th ed., Springfield, Ill: Charles C Thomas Pub Ltd, 2007, pp. 447–454.

[40] M. J. Kern, "Angiographic data," in *Cardiac Catheterization Handbook: Expert Consult - Online and Print, 5e*, 5th ed., Philadelphia, PA: Mosby, 2011, pp. 145–218.

[41] M. J. Kern, *Cardiac Catheterization Handbook: Expert Consult - Online and Print, 5e*, 5th ed. Philadelphia, PA: Mosby, 2011.

[42] C. Di Mario and N. Sutaria, "Coronary angiography in the angioplasty era: projections with a meaning," *Heart*, vol. 91, no. 7, pp. 968–976, Jul. 2005.

[43] "CardiacCathPro.com." [Online]. Available: http://cardiaccathpro.com/CAD.html. [Accessed: 02-Dec-2016].

[44] S. C. Smith *et al.*, "ACC/AHA guidelines for percutaneous coronary intervention (Revision of the 1993 PTCA Guidelines)—executive summary A report of the american college of cardiology/american heart association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) Endorsed by the society for cardiac angiography and interventions," *Circulation*, vol. 103, no. 24, pp. 3019–3041, Jun. 2001.

[45] L. W. Klein and R. J. Krone, "Cardiac interventions today - angiographic characterization of lesion morphology," *Cardiac Interventions Today*, 2008.08-2008. [Online]. Available: http://citoday.com/2008/08/CIT0808_07.php/. [Accessed: 22-Mar-2016].

[46] O. Tayeh and F. Ettori, "Vascular access and angiographic lesion morphology in elective percutaneous coronary intervention," *Egypt. Heart J.*, vol. 66, no. 1, pp. 27–33, Mar. 2014.

[47] S. Tu *et al.*, "Coronary angiography enhancement for visualization," *Int. J. Cardiovasc. Imaging*, vol. 25, no. 7, pp. 657–667, Oct. 2009.

[48] M. A. U. Khan, M. K. Khan, and M. Aurangzeb Khan, "Coronary angiogram image enhancement using decimation-free directional filter banks," in *IEEE International Conference on Acoustics, Speech, and Signal Processing, 2004. Proceedings. (ICASSP '04)*, 2004, vol. 5, pp. V–441–4 vol.5.

[49] P. T. H. Truc, M. A. U. Khan, Y.-K. Lee, S. Lee, and T.-S. Kim, "Vessel enhancement filter using directional filter bank," *Comput Vis Image Underst*, vol. 113, no. 1, pp. 101–112, Jan. 2009.

[50] C. Köse, "Fully automatic segmentation of coronary vessel structures in poor quality x-ray angiogram images," in *Structural, Syntactic, and Statistical Pattern Recognition*, D.-Y. Yeung, J. T. Kwok, A. Fred, F. Roli, and D. de Ridder, Eds. Springer Berlin Heidelberg, 2006, pp. 74–82.

[51] S. Tu, Y. Wu, X. Lu, H. Huo, and T. Fang, "Stick-guided lateral inhibition for enhancement of low-contrast image," 2007, vol. 6788, p. 67881W–67881W–8.

[52] C. Xiao, S. Zhang, S. Cheng, and Y. Chen, "A novel method for speckle reduction and edge enhancement in ultrasonic images," 2005, vol. 5637, pp. 469–476.

[53] M. A. U. Khan, R. Bahadur Khan, S. Bilal, A. Jamil, and M. Ali Shah, "Enhancement of angiogram images using pseudo color processing," *Inf. Technol. J.*, vol. 7, no. 1, pp. 210–214, Jan. 2008.

[54] D. S. D. Lara, A. W. C. Faria, A. de A. Araújo, and D. Menotti, “A novel hybrid method for the segmentation of the coronary artery tree in 2D angiograms,” *Int. J. Comput. Sci. Inf. Technol. IJCSIT*, vol. 5, no. 3, pp. 45–65, Jun. 2013.

[55] H. S. S. Ahmed and J. Nordin, “Improving diagnostic viewing of medical images using enhancement algorithms,” *J. Comput. Sci.*, vol. 7, no. 12, pp. 1831–1838.

[56] N. M. Sasi and V. K. Jayasree, “Contrast limited adaptive histogram equalization for qualitative enhancement of myocardial perfusion images.,” *Engineering*, vol. 5, pp. 326–331, 2013.

[57] A. Kusumawardhani, T. Mengko, I. Fahri, S. Soerianata, D. Firman, and H. Zakaria, “Coronary angiogram stabilization for QuBE values calculation using SIFT method,” in *2011 2nd International Conference on Instrumentation, Communications, Information Technology, and Biomedical Engineering (ICICI-BME)*, 2011, pp. 111–116.

[58] S. Zheng and D. Weirong, “Analysis of coronary arterial dynamics from x-ray angiographic sequences,” presented at the Second International Symposium on Computational Intelligence and Design, Changsha, 2009, vol. 1, pp. 201–204.

[59] R. C. Gonzalez and R. E. Woods, “Image segmentation,” in *Digital Image Processing*, 3rd ed., Addison-Wesley Pub (Sd), 1992, pp. 689–794.

[60] C. Kirbas and F. K. H. Quek, “Vessel extraction techniques and algorithms: a survey,” in *Third IEEE Symposium on Bioinformatics and Bioengineering, 2003. Proceedings*, 2003, pp. 238 – 245.

[61] R. M. Tayebi *et al.*, “Coronary artery segmentation in angiograms with pattern recognition techniques – a survey,” in *2013 International Conference on Advanced Computer Science Applications and Technologies (ACSAT)*, 2013, pp. 321–326.

[62] A. Dogra and P. Bhalla, “Image sharpening by gaussian and butterworth high pass filter,” *Biomed Pharmacol. J.*, vol. 7, no. 2, pp. 707–713, 2014.

[63] A. F. Frangi, W. J. Niessen, K. L. Vincken, and M. A. Viergever, “Multiscale vessel enhancement filtering,” in *Medical Image Computing and Computer-Assisted Interventation — MICCAI’98*, W. M. Wells, A. Colchester, and S. Delp, Eds. Springer Berlin Heidelberg, 1998, pp. 130–137.

[64] S. Wang, B. Li, and S. Zhou, “A segmentation method of coronary angiograms based on multi-scale filtering and region-growing,” in *2012 International Conference on Biomedical Engineering and Biotechnology (iCBEB)*, 2012, pp. 678–681.

[65] D. S. D. Lara, A. W. C. Faria, A. de A Araujo, and D. Menotti, “A semi-automatic method for segmentation of the coronary artery tree from angiography,” in *2009 XXII Brazilian Symposium on Computer Graphics and Image Processing (SIBGRAPI)*, 2009, pp. 194–201.

[66] K. Zuiderveld, *Graphics Gems IV*. San Diego, CA, USA: Academic Press Professional, Inc., 1994.

[67] Shashank, M. Bhattacharya, and G. K. Sharma, “Optimized coronary artery segmentation using frangi filter and anisotropic diffusion filtering,” in *2013 International Symposium on Computational and Business Intelligence (ISCBI)*, 2013, pp. 261–264.

[68] G. Sasidharan and A. George, “Frangi’s vessel detection approach for coronary angiogram segmentation,” *Int. J. Eng. Trends Technol.*, vol. 13, no. 5, pp. 213–217, Jul. 2014.

[69] J. F. O’Brien and N. F. Ezquerra, “Automated segmentation of coronary vessels in angiographic image sequences utilizing temporal, spatial, and structural constraints,” 1994, vol. 2359, pp. 25–37.

[70] R. C. Gonzalez and R. E. Woods, “Morphological image processing,” in *Digital Image Processing*, 3rd ed., Addison-Wesley Pub (Sd), 1992, pp. 627–687.

[71] S. Eiho and Y. Qian, “Detection of coronary artery tree using morphological operator,” in *Computers in Cardiology 1997*, 1997, pp. 525–528.

[72] T.-F. Lee, C.-Y. Lee, P.-J. Chao, C. Lee, C.-Y. Wang, and C.-H. Fang, “Quantitative coronary analysis medical image processing improved by combining wavelet edge detection and segmentation,” in *2009 Fourth International Conference on Innovative Computing, Information and Control (ICICIC)*, 2009, pp. 1196–1199.

[73] C. Kirbas and F. Quek, “A review of vessel extraction techniques and algorithms,” *ACM Comput Surv*, vol. 36, no. 2, pp. 81–121, Jun. 2004.

[74] S. Nirmala Devi and N. Kumaravel, “Comparison of active contour models for image segmentation in X-ray coronary angiogram images,” *J. Med. Eng. Technol.*, vol. 32, no. 5, pp. 408–418, Jan. 2008.

[75] P. Zou, P. Chan, and P. Rockett, “A model-based consecutive scanline tracking method for extracting vascular networks from 2-D digital subtraction angiograms,” *IEEE Trans. Med. Imaging*, vol. 28, no. 2, pp. 241–249, 2009.

[76] P. M. J. van der Zwet, I. M. F. Pinto, P. W. Serruys, and J. H. C. Reiber, “A new approach for the automated definition of path lines in digitized coronary angiograms,” *Int. J. Card. Imaging*, vol. 5, no. 2, pp. 75–83, 1990.

[77] Z. Shoujun, Y. Jian, W. Yongtian, and C. Wufan, “Automatic segmentation of coronary angiograms based on fuzzy inferring and probabilistic tracking,” *Biomed. Eng. OnLine*, vol. 9, no. 1, p. 40, Aug. 2010.

[78] S. A. Stansfield, “ANGY: A rule-based expert system for automatic segmentation of coronary vessels from digital subtracted angiograms,” *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. PAMI-8, no. 2, pp. 188 –199, Mar. 1986.

[79] S. D. Tomasello and C. Luca, “Quantitative coronary angiography in the interventional cardiology,” in *Advances in the Diagnosis of Coronary Atherosclerosis*, InTech, 2011, pp. 255–270.

[80] J. Canny, “A computational approach to edge detection,” *IEEE Trans Pattern Anal Mach Intell*, vol. 8, no. 6, pp. 679–698, Jun. 1986.

[81] A. Hernandez-Vela *et al.*, “Accurate coronary centerline extraction, caliber estimation, and catheter detection in angiographies,” *IEEE Trans. Inf. Technol. Biomed.*, vol. 16, no. 6, pp. 1332–1340, Nov. 2012.

[82] W. Yumei, “Tracking of coronary arteries in angiogram sequence by structural matching of junctions,” Thesis, 2011.

[83] T. Y. Zhang and C. Y. Suen, “A fast parallel algorithm for thinning digital patterns,” *Commun ACM*, vol. 27, no. 3, pp. 236–239, Mar. 1984.

[84] K. Haris, S. N. Efstratiadis, N. Maglaveras, J. Gourassas, C. Pappas, and G. Louridas, “Coronary arterial tree extraction based on artery tracking and mathematical morphology,” in *Computers in Cardiology 1998*, 1998, pp. 769–772.

[85] K. Haris, S. N. Efstratiadis, N. Maglaveras, C. Pappas, J. Gourassas, and G. Louridas, “Model-based morphological segmentation and labeling of coronary angiograms,” *IEEE Trans. Med. Imaging*, vol. 18, no. 10, pp. 1003–1015, Oct. 1999.

[86] Y. Sun, “Automated identification of vessel contours in coronary arteriograms by an adaptive tracking algorithm,” *IEEE Trans. Med. Imaging*, vol. 8, no. 1, pp. 78–88, Mar. 1989.

[87] A. K. Klein, F. Lee, and A. A. Amini, “Quantitative coronary angiography with deformable spline models,” *IEEE Trans. Med. Imaging*, vol. 16, no. 5, pp. 468–482, Oct. 1997.

[88] P. Bifulco, M. Romano, M. Cesarelli, L. Iuppariello, and N. Pasquino, “Estimation of quantum noise in fluoroscopy by analyzing differences of static images,” presented at the 20th ImeKo TC-4 International Symposium, 2014, pp. 790–793.

[89] Z. Sun and Y. Zhou, “Assessing cardiac dynamics based on X-ray coronary angiograms,” *J. Multimed.*, vol. 8, pp. 48–55, Feb. 2013.

[90] F. Moscheni, F. Dufaux, and M. Kunt, “A new two-stage global/local motion estimation based on a background/foreground segmentation,” in *1995 International Conference on Acoustics, Speech, and Signal Processing, 1995. ICASSP-95*, 1995, vol. 4, pp. 2261–2264 vol.4.

[91] D. L. Bhatt, “Noise,” in *Cardiovascular Intervention: A Companion to Braunwald’s Heart Disease*, Elsevier Health Sciences, 2015, p. 99.

[92] P. Kalra and S. Peleg, “Fingerprint image enhancement,” in *Computer Vision, Graphics and Image Processing: 5th Indian Conference, ICVGIP 2006, Madurai, India, December 13-16, 2006, Proceedings*, Springer, 2007, pp. 951–961.

[93] R. C. Gonzalez, “Homomorphic filtering,” in *Digital Image Processing*, Pearson Education India, 2009, pp. 311–315.

[94] E. H. W. Meijering, K. J. Zuiderveld, and M. A. Viergever, “Image registration for digital subtraction angiography,” *Int. J. Comput. Vis.*, vol. 31, no. 2–3, pp. 227–246, Apr. 1999.

[95] G. Bradski and A. Kaehler, “Template matching,” in *Learning OpenCV: Computer Vision with the OpenCV Library*, 1st ed., O’Reilly Media, 2008, pp. 214–219.

[96] N. Dalal and B. Triggs, “Histograms of oriented gradients for human detection,” in *2005 IEEE Computer Society Conference on Computer Vision and Pattern Recognition (CVPR’05)*, 2005, vol. 1, pp. 886–893 vol. 1.

[97] K. A. S. H. Kulathilake, L. Ranathunga, G. R. Constantine, and N. A. Abdullah, “Region growing segmentation method for extracting vessel structures from coronary cine-angiograms,” in *Moratuwa Engineering Research Conference (MERCon), 2015*, 2015, pp. 142–147.

[98] K. A. S. H. Kulathilake, L. Ranathunga, G. R. Constantine, and N. A. Abdullah, “A segmentation method for extraction of main arteries from coronary cine-angiograms,” in *2015 Fifteenth International Conference on Advances in ICT for Emerging Regions (ICTer)*, 2015, pp. 9–15.

[99] A. C. Bovik, “Canny’s method,” in *Handbook of Image and Video Processing*, Academic Press, 2010, pp. 548–549.

[100] J. T. Dodge, B. G. Brown, E. L. Bolson, and H. T. Dodge, “Lumen diameter of normal human coronary arteries. Influence of age, sex, anatomic variation, and left ventricular hypertrophy or dilation.,” *Circulation*, vol. 86, no. 1, pp. 232–246, Jul. 1992.

[101] K. Kaur and N. Gupta, “Evaluating the performancne of DBLA Using CLAHE & dark channel prior,” *Int. J. Adv. Res. Comput. Sci. Softw. Eng.*, vol. 5, no. 5, pp. 960–969, May 2015.

APPENDIX A: STRENGTH AND LIMITATION ANALYSIS OF CARDIAC MEDICAL IMAGE MODALITIES

Image Modality	Strength	Limitations
Stress echo-cardiography	It is a low cost method. Global and regional left and right ventricular systolic function, valvular disease and hemodynamic can be assessed quickly and with reasonable accuracy.	A proportion of patients have inadequate or suboptimal images. The success of imaging varies from laboratory to laboratory and dependent on the sonographer expertise, physicians' proficiency and tolerance for technically difficult studies (e.g., obese patients). In approximately 10–20% of examinations, two or more of 16 (or 17) myocardial segments may not be well visualized.
SPECT	Provides physiological information through functional imaging. Can detect metabolic activity blood flow, intrinsic lesion localization	Gamma emissions harmful to the patients. Non-hybrid devices have poor spatial resolution. Tissue boundaries are ill-determined Longer scanning duration, exceeding 30-40 minutes
PET	It allows study of body functions and can help physicians detect alterations in biochemical processes that imply the possibility of diseases before changes in anatomy are detected using other imaging tests, such as CT or MRI. As the radioactivity is very short-lived, patients' exposure to radiation is low.	Time-consuming. The resolution of structures of the body with nuclear medicine may not be as clear as with other imaging techniques, such as CT or MRI.PET scanning can give false results if chemical balances within the body are not normal.A person who is very obese may not fit into the opening of a conventional PET/CT unit.

Image Modality	Strength	Limitations
Cardiac MRI	MRI does not have any ionizing radiation, thus permitting its use in children and pregnant women. It can produce high resolution and 3D images of the cardiac chambers and thoracic vessels. Unlike echocardiography, MRI can produce images of cardiovascular structures without interference from adjacent bone or air, which limits echocardiography. MRI is also less operator dependant than echocardiography.Velocity encoded techniques permit measurement of blood flow. MRI does not have the weakness of geometric assumptions (as do angiography and 2D echo-cardiography) in assessing ventricular volumes.	MRI requires more patient cooperation than other tests and claustrophobic patients may not be able to undergo the exam. The duration of examination is significantly longer compared with CT. Installation and operation of MRI equipment is costly. MRI has less spatial resolution than CT, which limits the evaluation of small structures such as the CAs.
MSCT	Small and rapidly moving anatomic structures could be visualized with good image quality. Coronary CT angiography investigation allows the accurate detection of CA stenosis. 3D imaging provides a real coronary mapping mode using 3D volume rendering.Cardiac CT has the potential to visualize earlier stages of coronary atherosclerosis.CT provides for accurate assessment of general cardiac morphology.	Compared to other diagnostic tests, CT scans deliver a relatively high dose of radiation to the patient. Allergic Reaction due to the contrast agents.

Image Modality	Strength	Limitations
X-ray angiography	Provide excellent visualizations of CA vasculature. Low cost.	It consists of some visual artifacts, which causes degradations such as; non-uniform illumination, noise. It provides only two dimensional images. Difficult to quantitatively analyze the CAs lumen. Subjective analysis leads to over estimations and under estimations of detected stenosis.
IVUS	IVUS enables a physician to detect inside the artery with a camera-like device. IVUS can quantify the percentage of narrowing and give insights into the nature of the plaque.	Some artifacts that occur during imaging causes erroneous results; e.g. ring-down artifact, nurd. The real three-dimensional geometry can hardly be obtained. IVUS is normally applied to a short segment of the vessel to minimize complications in the catheterization procedure, and it is almost impossible to image every branch of the coronary tree in order to recover the complete shape.
OCT	Provides accurate measurement of the structures in the vasculature than IVUS. Images contain broad dynamic range and high resolution. It can be used to determine the morphology of detected plaques.	The real three-dimensional geometry can hardly be obtained. OCT is normally applied to a short segment of the vessel to minimize complications in the catheterization procedure, and it is almost impossible to image every branch of the coronary tree in order to recover the complete shape.
FFR	Provides accurate measurements of the stenosis based on the functional significance.	The pressure wire used for the FFR is costly.

APPENDIX B: PSEUDO CODE OF SKELETON PATH TRACKER

Skeleton Path Tracker (seedPoint)

```
BEGIN

        skeletonPointArray []

        taggedPointArray[]

        candidateKeyArray[]

        candidateKeyDensityArray[]

        trackingStatus ←1

        kpCount, taggedCount, candidateCount, candidateDensityCount ←0

        currentSeedPoint ← seedPoint

        skeletonPointArray[kpCount] ← currntSeedPoint

        WHILE (trackingStatus ==1)

          FOR EACH 8 neighbors of currentSeedPoint

            IF (pixelValue == 255 && notVisited && notTagged) THEN

              skeletonPointArray[++kpCount] ← neighborPoint

              candidateKeyArray[candidateCount++] ← neighborPoint

           END IF

          END FOR

          IF (candidateCount == 0) THEN

            taggedPointArray [++taggedCount] ←currentSeedPoint

            trackingStatus ←0

          ELSE IF (candidateCount == 1) THEN
```

```
    taggedPointArray [++taggedCount]← currentSeedPoint
    currentSeedPoint ← candidateKeyArray[0]
    re-set candidateKeyArray
ELSE
    FOR EACH candidateKey point in candidateKeyArray
        count ←0
        FOR EACH 8 neighbors of candidateKey point in candidateKeyArray[]
            IF (pixelValue == 255 && notTagged && !currnetSeedPoint) THEN
                count++
                candidateKeyDensityArray [candidateKeyDensityCount++] ← count
            END IF
        END FOR
    END FOR
max ←0;
maxIndex ←0;
FOR (n ← 0; n< candidateCount)
    IF(max<= candidateKeyDensityArray[n]) THEN
        max ← candidateKeyDensityArray[n]
        maxIndex ← n
    END IF
END FOR
taggedPointArray [++taggedCount]← currentSeedPoint
FOR(n ← 0; n< candidateCount)
```

```
        IF( n!= maxIndex) THEN
          taggedPointArray [++taggedCount] ←candidateKeyArray[n]
        END IF
      END FOR
      currentSeedPoint ← candidateKeyArray[maxIndex]
      re-set candidateKeyArray
    END WHILE
END
```

Note:

notVisited indicates that the pixel point is not exists in skeletonPointArray[] and **notTagged** indicates that the pixel point is not exists in taggedPointArrayp[].

Following section elaborates the execution steps of Skeleton Path Tracker algorithm by using a sample skeleton image.

Example:

Following Figure A depicts a sample skeleton image and seed point is given as [5,2]. Arrow head in the Figure A indicates the tracking direction. Table A enlists the steps of the proposed Skeleton Path Tracker algorithm and each column in the table represents the values, which are manipulated in accordance with the execution steps.

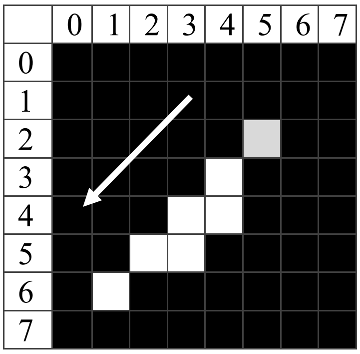


Figure A – Sample skeleton image

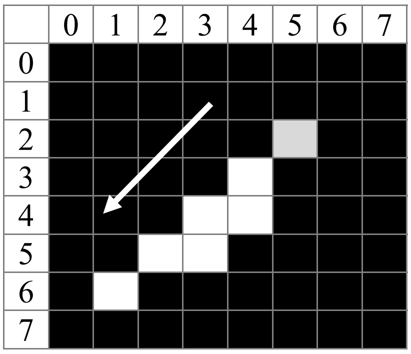
Skeleton Point Array	[5,2]	[4,3]	[3,4]	[4,4]	[2,5]	[3,5]	[1,6]

Tagged Point Array	[5,2]	[4,3]	[4,4]	[3,4]	[3,5]	[2,5]	[1,6]

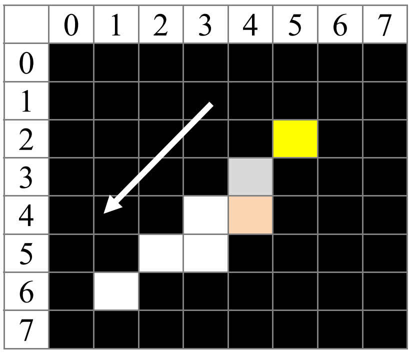
Table A: Steps of the proposed Skeleton Path Tracker algorithm

Iterations	Iteration 1	Iteration 2	Iteration 3	Iteration 4	Iteration 5
Current seed point	[5,2]	[4,3]	[3,4]	[2,5]	[1,6]
White colored 8 Neighbors	[4,3]	[5,2][3,4] [4,4]	[4,3] [4,4] [2,5] [3,5]	[3,4] [3,5] [1,6]	[2,5]
Key Found status	0	1,0,0	1,1,0,0	1,1,0	1
Tagged status	0	1,0,0	1,1,0,0	1,1,0	1
Add to Skeleton Point array	[4,3]	[3,4] [4,4]	[2,5] [3,5]	[1,6]	-
Selected Candidate Key Points	[4,3]	[3,4] [4,4]	[2,5] [3,5]	[1,6]	-
Selected Candidate Key count	1	2	2	1	0
Case Number	2	3	3	2	1
End tracking	No	No	No	No	Yes
Candidate Density count	-	3,2	2,1	-	
Maximum density value	-	3	2	-	
Maximum density index	-	0	0	-	
Tagged → current seed point and non-maximum density Candidate Key points	[5,2]	[4,3], [4,4]	[3,4][3,5]	[2,5]	[1,6]
Next seed point → maximum indexed Candidate Key point	[4,3]	[3,4]	[2,5]	[1,6]	-

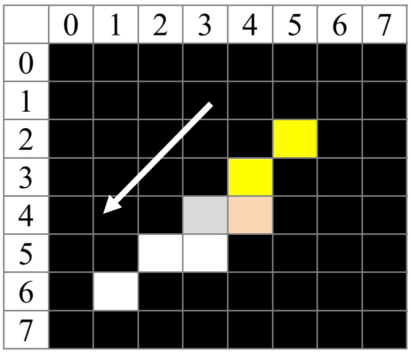
Following diagrams visually illustrate the skeleton path tracking progress according to the iterations. Gray colored pixel depicts the seed point. Yellow colored pixels represent the tracked key points. Orange colored pixels represent the tagged candidate pixels. Arrow head in each diagram indicates the tracking direction.



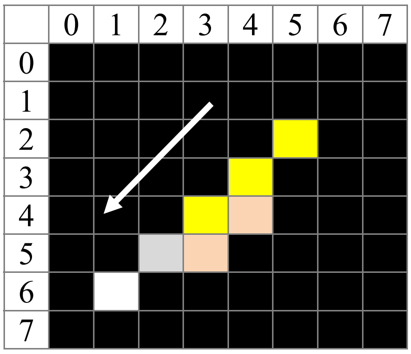
Iteration 1



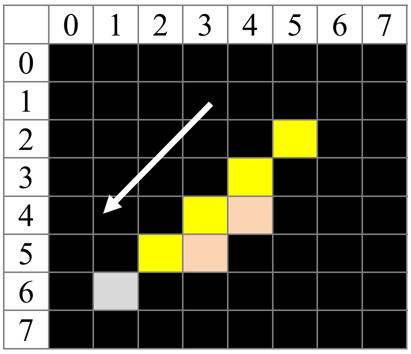
Iteration 2



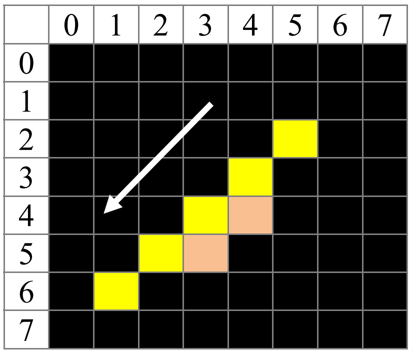
Iteration 3



Iteration 4



Iteration 5

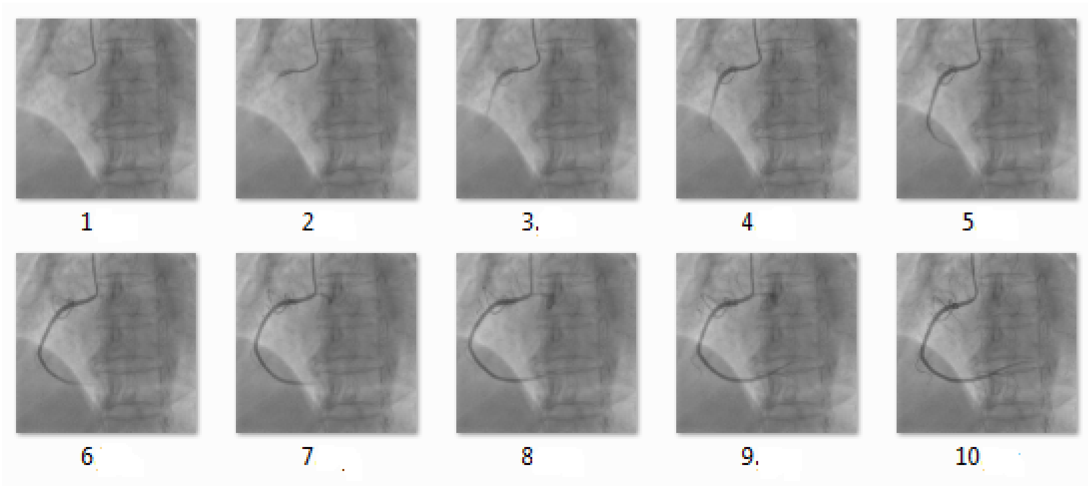


End of tracking

APPENDIX C: VISUAL ILLUSTRATIONS OF PROCESSING STEPS

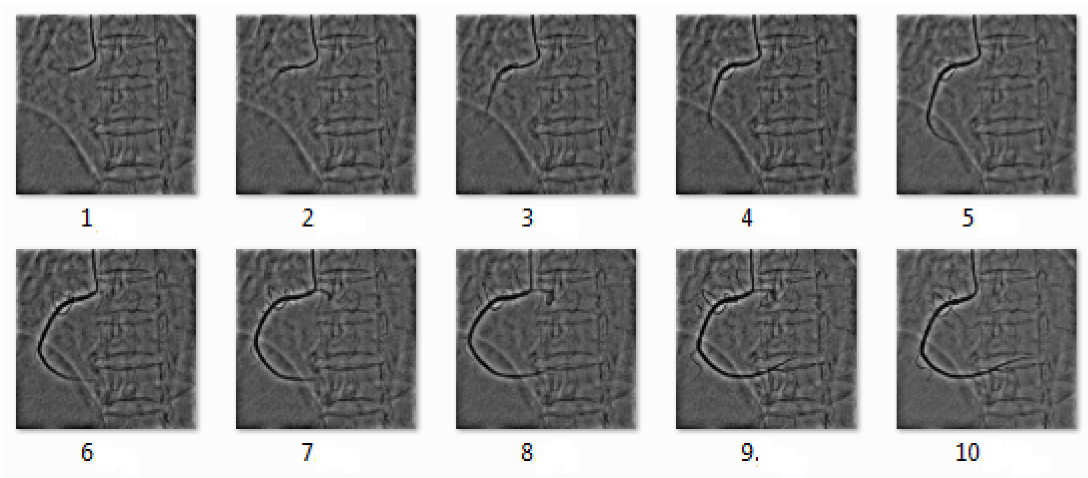
The visual illustrations of the processing steps of the proposed methodology have been presented in this section. A sample CCA of RCA recorded under LAO cranial view has been selected and it consists of 10 frames to be processed.

Original frames ($f_0(x,y)$) of the selected video



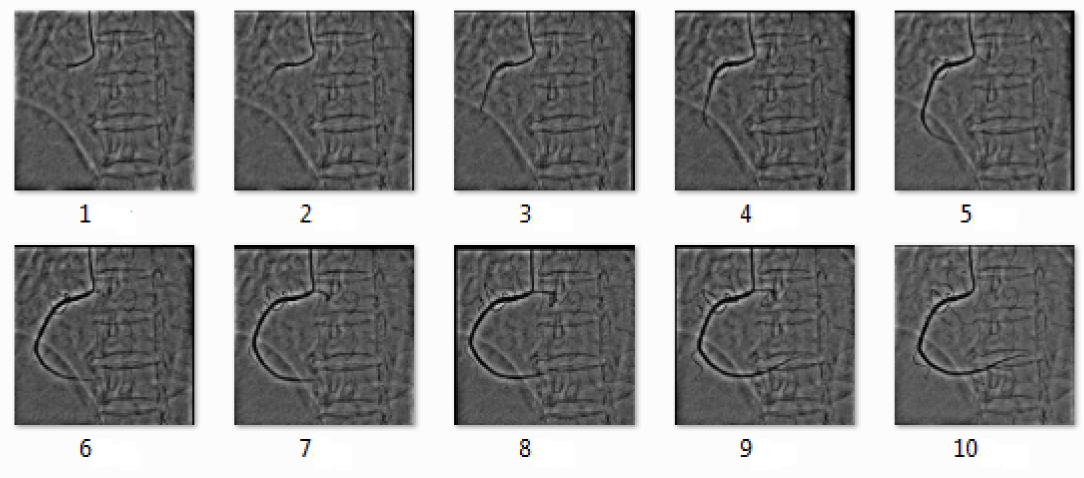
Enhanced Frames ($f_3(x,y)$)

Following are the uniformly illuminated normalized frames.



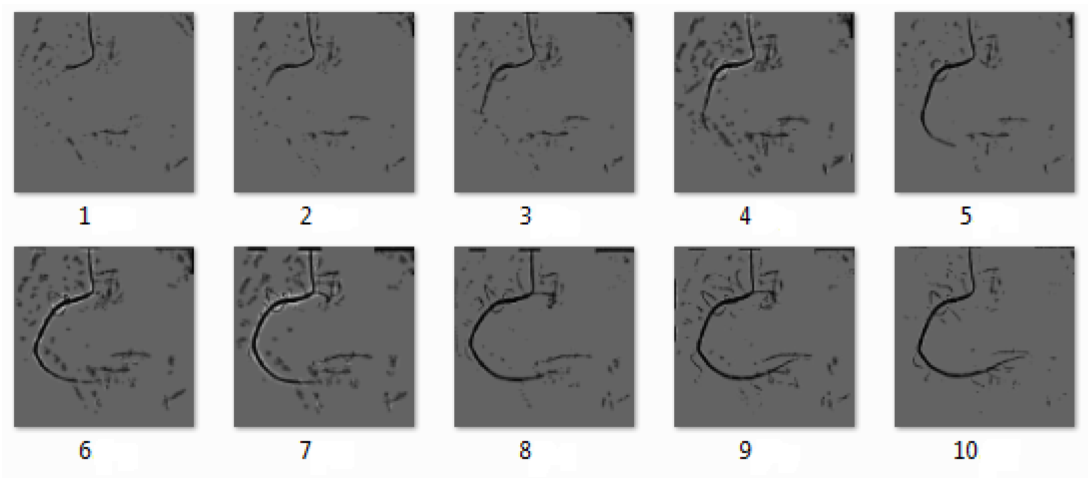
Aligned Frames ($f_4(x,y)$)

Following set of frames can be obtained after reduction of global motion from the enhanced frames.



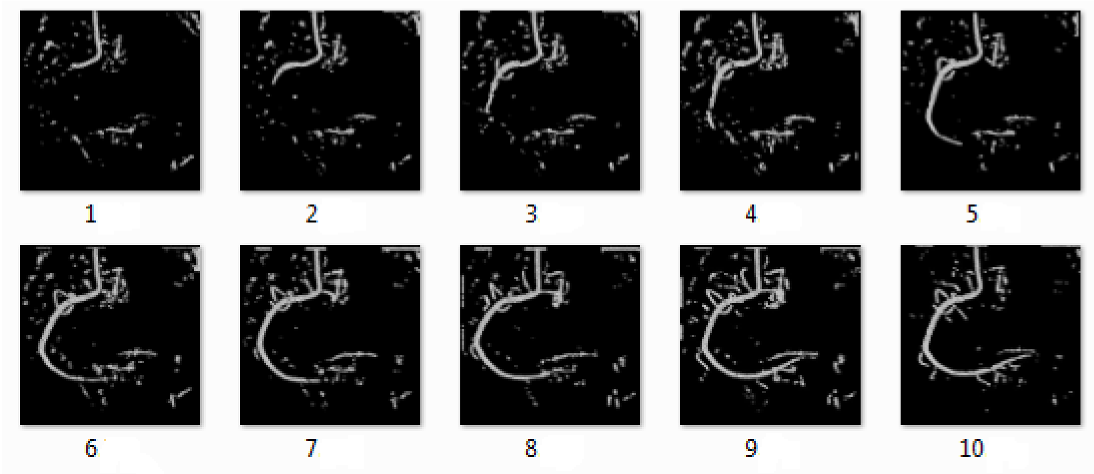
Background subtraction ($f_5(x,y)$)

Following set of frames can be obtained after subtracting the created mask image from each and every aligned frame. As a consequence of the operation the foreground area has been emphasized.



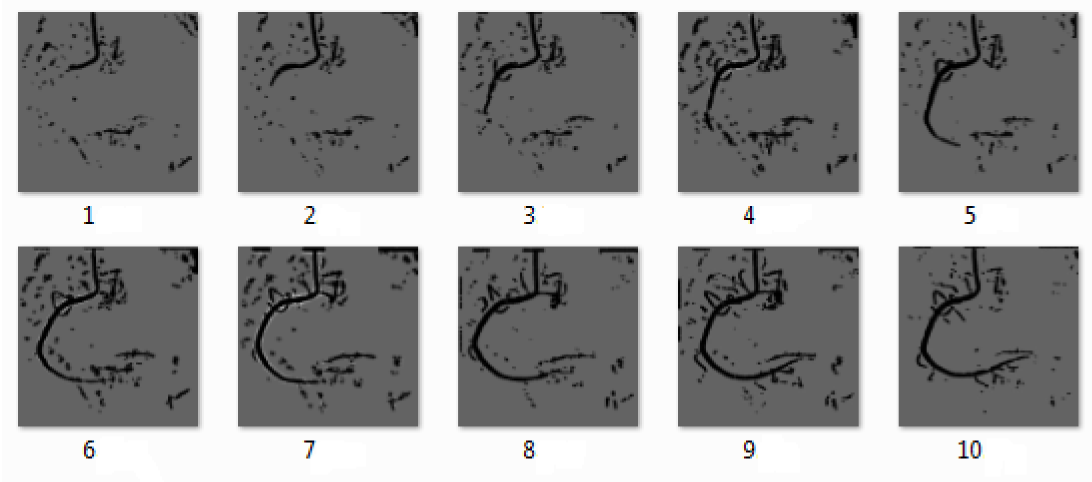
Foreground enhanced frames ($f_6(x,y)$)

Application of Frangi's vessel enhancement filter emphasizes the tubular structures of the CCAs and can be used to determine the vesselness feature of the frames.



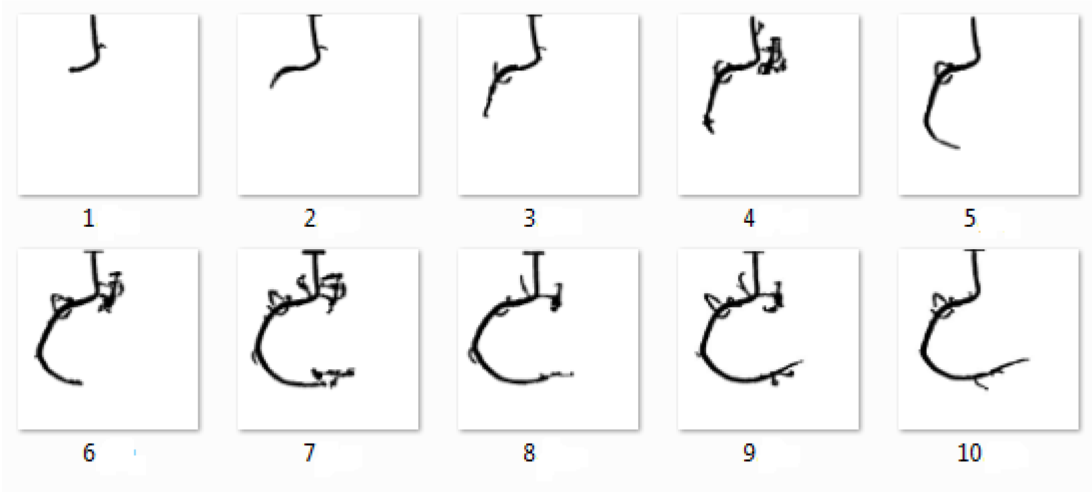
Overlapped and normalized frames ($f_7(x,y)$)

Following frames are obtained as a result of application of structure filling and normalization operations. These operations improve the special coherence of the vessel structures and represent them with uniform intensity.



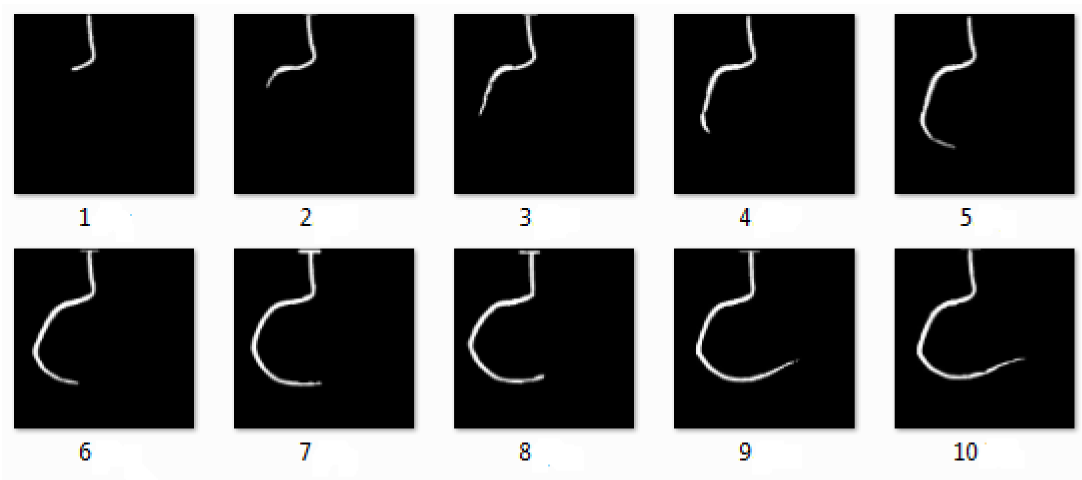
Foreground extracted frames ($f_8(x,y)$)

Following frames provide visual illustrations to emphasize the segmentation results of the processed CCA.

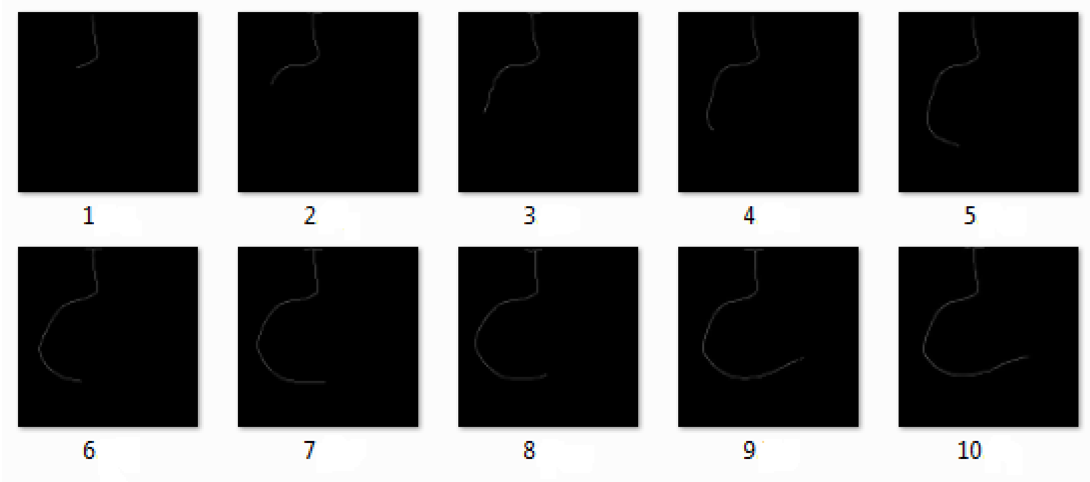


Vessel isolation ($f_9(x,y)$)

The root arterial segments of the RCA selected to be isolated have been depicted in the frames.



Skeleton ($f_s(x,y)$)



APPENDIX D: RESULTS OF CLINICAL FEASIBILITY ANALYSIS OF PROPOSED METHOD

Following table enlists the results of the clinical feasibility analysis of the proposed method. Selected CCA are listed in CCA case ID column and the English letter of each case indicates the name of the diagnosed CA. Hence, ‘R’ indicates the RCA, ‘L’ indicates LCA and ‘C’ indicates the CX artery. Subjective analysis results are directly extracted from the clinical reports, which belong to these patient cases and objective analysis results are computed by the quantitative coronary analysis method proposed in this study. Severity level of both subjective results and objective results are determined according to the criteria mentioned in section 6.4.2.

CCA case ID	Subjective Analysis Result	Severity Level	Objective Analysis Result	Severity Level	Stenosis Location
3883R	90	Severe	79.18	Severe	Mid
4233R	90	Severe	57.47	Moderate	Proximal
4538R	99	Total Occlusion	75.60	Severe	Mid
4585R	70	Moderate	74.19	Moderate	Mid long lesion
4782R	90	Severe	60.00	Moderate	Proximal mid long lesion
4837R	40	Minimal	65.20	Moderate	Diffuse disease
5088R	90	Severe	57.29	Moderate	Proximal
5339R	95	Severe	79.83	Severe	Proximal
5371R	50	Moderate	44.19	Minimal	Proximal
5438R	70	Moderate	59.36	Moderate	Mid
5713R	99	Total Occlusion	72.33	Moderate	Mid

CCA case ID	Subjective Analysis Result	Severity Level	Objective Analysis Result	Severity Level	Stenosis Location
4234L	99	Total Occlusion	54.98	Moderate	Mid culprit lesion
4585L	40	Minimal	38.90	Minimal	Mid
4645L	90	Severe	66.80	Moderate	Proximal
4646L	40	Minimal	62.49	Moderate	Proximal
5084L	99	Total Occlusion	71.15	Moderate	Mid
5088L	90	Severe	20.00	Minimal	Proximal
5106L	90	Severe	64.09	Moderate	Proximal
5233L	70	Moderate	65.00	Moderate	Proximal
5328L	80	Severe	88.55	Severe	Mid
5339L	70	Moderate	35.71	Minimal	After d1
5371L	40	Minimal	33.67	Minimal	Proximal
5438L	99	Total Occlusion	54.70	Moderate	Proximal
5473L	90	Severe	82.00	Severe	Proximal
5556L	50	Moderate	68.60	Moderate	Proximal
4233C	70	Moderate	30.28	Minimal	Proximal
4434C	70	Moderate	49.53	Minimal	Obtuse marginal
4645C	70	Moderate	52.60	Moderate	Proximal
4646C	65	Moderate	55.87	Moderate	Ostial
4650C	70	Moderate	78.25	Severe	Proximal
4969C	60	Moderate	56.69	Moderate	Proximal

CCA case ID	Subjective Analysis Result	Severity Level	Objective Analysis Result	Severity Level	Stenosis Location
5067C	45	Minimal	50.42	Moderate	Proximal
5556C	50	Moderate	52.30	Moderate	Proximal

APPENDIX E: PUBLICATIONS BASED ON THIS RESEARCH STUDY

Peer Reviewed Journal Article

K. A. S. H. Kulathilake, L. Ranthunga, G. Constantine, and N. A. Abdulla, "Hierarchical region based template matching technique for global motion reduction of coronary cineangiograms," *Int. J. Comput. Theory Eng.*, 7(2), pp. 156–161, 2014.

Kulathilake, K.A.S.H., Ranthunga, L., Constantine, G., Abdullah, "Visual alignment of arteries in coronary cine-angiogram using global motion stabilization approach." in J. National Science Foundation, 45(1), pp.41–51, 2017

Book Chapter

K. A. S. H. Kulathilake, L. Ranathunga, G. R. Constantine, and N. A. Abdullah, "Reduction of motion disturbances in coronary cineangiograms through template matching," in *Future Information Technology*, J. J. (Jong H. Park, Y. Pan, C.-S. Kim, and Y. Yang, Eds. Springer Berlin Heidelberg, 2014, pp. 267–273.

IEEE Indexed Conference Publications

K. A. S. H. Kulathilake, L. Ranathunga, G. R. Constantine, and N. A. Abdullah, "Region growing segmentation method for extracting vessel structures from coronary cine-angiograms," in *Moratuwa Engineering Research Conference (MERCon)*, 2015, pp. 142–147.

K. A. S. H. Kulathilake, L. Ranathunga, G. R. Constantine, and N. A. Abdullah, "A segmentation method for extraction of main arteries from Coronary Cine-Angiograms," in *2015 Fifteenth International Conference on Advances in ICT for Emerging Regions (ICTer)*, 2015, pp. 9–15.

K. A. S. H. Kulathilake, L. Ranathunga, G. R. Constantine, and N. A. Abdullah, "Computing lumen diameter of coronary arteries using segmented vessel's geometry and line tracking," in *2016 International Conference on Information Science (ICIS)*, 2016, pp. 109–115.

K. A. S. H. Kulathilake, L. Ranathunga, G. R. Constantine, and N. A. Abdullah, "A technique for quantitative coronary analysis of cine-angiograms using segmentation and vessel path tracking", i*n 2016 International Conference on Advances in ICT for Emerging Regions (ICTer)*, 2016. pp.87-95.