CT Liver Protocol Audit:

Assessment of Cirrhotic Liver Enhancement with Multiphasic CT Using a Faster Injection Rate, Late Arterial Phase, & Weight-Based Contrast Dosing

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Disclosures

- None

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Background

- Hepatocellular carcinoma (HCC) is one of the leading causes of cancer related death worldwide
- In North America, the incidence of HCC has tripled over the past 30 years
- Incidence is projected to continue rising due to increasing rates of chronic liver diseases
- Alcohol & obesity-related cirrhosis on the rise
- The vast majority of HCC arises in cirrhotic livers

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References 1,2

Background

- American Association for the Study of Liver Diseases (AASLD) 2010 Guidelines recommend surveillance with ultrasound every 6 months in patients with cirrhosis or deemed high risk
- Diagnosis of HCC is usually made by multiphasic CT or MR
- Tissue diagnosis NOT needed if lesion meets imaging criteria
- Major implications in patient management
  - Direct effect on treatment, surgical intervention, transplant

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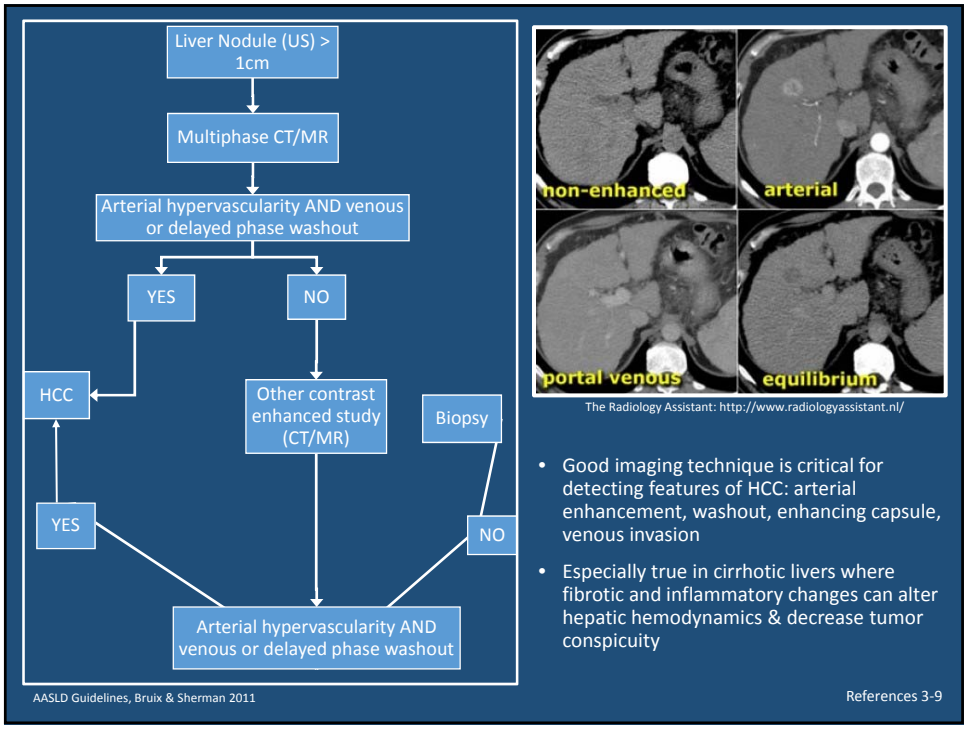
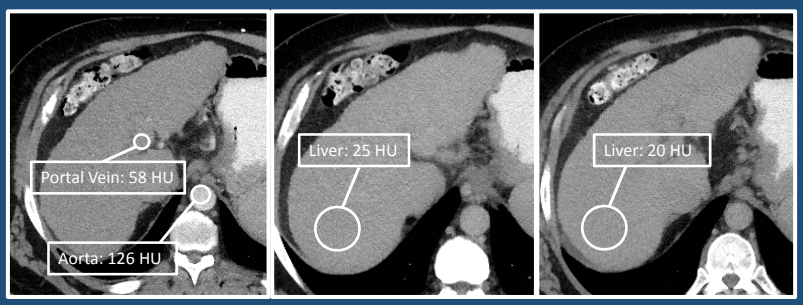
References 3-9



Background

- At our institution, fixed dose (100 mL of Isovue 370) liver CT examinations were resulting in poor liver enhancement

LOCAL CASE: 149 kg, 100 mL Isovue 370 @ 3 mL/s, early arterial phase
IODINE CONCENTRATION: 248 mg I/kg



Objectives

1. To quantitatively evaluate the effect of our CT liver protocol modifications according to established imaging quality criteria.

2. To update our CT liver protocol according to recommended guidelines:
   - American College of Radiology Liver Imaging Reporting and Data System (ACR LI-RADS)
   - Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS)

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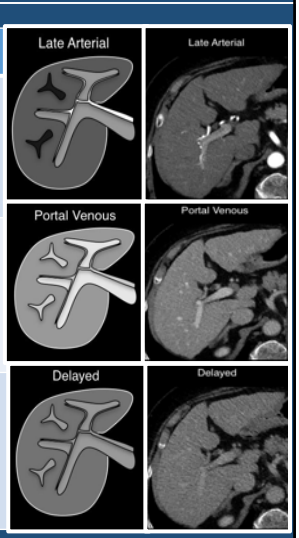
Standards

Phase	Recommended Parameters	Measure of Image Quality
Late Arterial Phase	• 3-5 mL/s x 30s[5,6,12,14] • 18-21 s post trigger	• Peak aortic attenuation 250-300 HU[13,23,24,29] • Avid portal vein[13,25,30] • Minimal liver enhancement (20-30 HU[23-25,30])
Portal Venous Phase	• Weight based contrast • Iodine concentration **500-750 mg I/kg**[6,10,12-14,24-26,28] • 30s post HAP (70-80s total delay)	• Liver enhancement ≥ **50 HU**[10,13,25] • Avid portal & hepatic veins[13,25]
Delayed Phase	• 3-5 min delay	• Maintain liver enhancement (close to 50 HU[25,31])



ACR LI-RADS & OPTN/UNOS

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Methods: Patient Selection

- As a quality assurance audit, Research Ethics Board approval waived
- Conducted at a single academic teaching hospital with subspecialty hepatobiliary surgery and liver transplantation service
- Patient selection:
  - FIRST CYCLE - "Old Protocol" Group: January 2015 – September 2015 all liver CT with imaging features of cirrhosis (n = 49)
  - SECOND CYCLE - "Modified Protocol" Group: October 2015 – December 2015 all liver CT with imaging features of cirrhosis (n = 31)
  - Only patients with documented liver cirrhosis or imaging signs of cirrhosis (parenchymal nodularity, lobar redistribution, widened fissures) included
  - Total of 4 studies were excluded due to pseudocirrhosis (n=2) or an unmeasurable, thrombosed portal vein (n=2)
- Patient age, gender, and weight obtained from electronic chart, iodine concentration calculated
- Clinical cirrhosis score (Model for End Stage Liver Disease, MELD) calculated from serum bilirubin, creatinine, and international normalized ratio

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Methods: CT Scanning Protocols

- CT examinations conducted on 1 of 3 scanners (Siemens Sensation 64, Definition AS+, and Definition Flash)
  - Sensation 64 not equipped with automated kV or mA

PHASE	FIRST CYCLE (OLD)	SECOND CYCLE (MODIFIED)
Late Arterial Phase	• 3 mL/s injection rate • EARLY arterial phase (10s post bolus triggering)	• 5 mL/s injection rate • LATE arterial phase (20s post bolus triggering)
Portal Venous Phase	• FIXED IV contrast dose (100 mL Isovue 370) • 75s total delay	• WEIGHT BASED IV contrast dose (1.7mL/kg Isovue 370, max 150mL) • 75s total delay
Delayed Phase	• 3 min delay	• 3 min delay

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Methods: Imaging Analysis

- Imaging Analysis
  - 4 phases: unenhanced (C-), late/hepatic arterial (HAP), portal venous (PVP), and equilibrium (EP)
  - All 4 phases analyzed, ROI's taken (KE):
    - Aorta at celiac axis
    - Main portal vein at porta hepatis
    - Liver parenchyma – average of 4 ROI's
    - Hepatic veins – average of all 3
- Peak attenuation of vessels recorded
- Enhancement of parenchyma calculated by subtracting unenhanced value from enhanced value

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Methods: Imaging Criteria & Statistics

Criteria	Phase/Standard	References
Liver enhancement	**PVP ≥50 HU**	10,13,25
Iodine concentration	**≥500 mg I/kg**	6,10,12-14,24-26,28
Peak aortic attenuation	HAP (≥250 HU)	13,23,24,29
Peak portal vein attenuation	HAP ("avid")	13,25,30
Liver enhancement	HAP (20-30 HU)	23-25,30
Peak hepatic vein attenuation	PVP ("avid")	13,25
Liver enhancement	EP (close to 50 HU)	25,31

- Primary standards for image quality:
  - **Liver enhancement in PVP ≥50 HU**
  - **Iodine concentration ≥500 mg I/kg**
- Statistical Analysis
  - Student T test to compare means of continuous variables
    - Patient age, weight, MELD score, enhancement values, iodine concentrations, and contrast to noise ratio (CNR)
  - Fisher's exact test used to compare number of males & females, number of suboptimal studies in each group

Results: Old Protocol

Criteria	Old Protocol	Suboptimal Studies	Phase/Standard	References
Liver enhancement (PVP)	51 ± 16 (n = 38)	**21/38 (<50 HU)**	≥50 HU	10,13,25
Iodine concentration (mg I/kg)	456 ±112 (248-822)	**9/11 (<500 mg I/kg)**	≥500 mg I/kg	6,10,12-14,24-26,28
Peak aorta (HAP)	242 ± 92		≥250 HU	13,23,24,29
Peak portal vein (HAP)	112 ± 41		"Avid"	13,25,30
Liver enhancement (HAP)	21± 12		20-30 HU	23-25,30
Peak hepatic vein (PVP)	144 ± 37		"Avid"	13,25
Liver enhancement (EP)	41 ± 15 (n = 27)		Close to 50 HU	25,31

TOTAL SUBOPTIMAL STUDIES: 30/49 (57%)

MODIFIED PROTOCOL:
- Weight based contrast dose (1.7 mL/kg)
- Faster injection rate (5 mL/s)
- Late arterial phase (20 s)

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Results: Modified Protocol

CLINICAL PARAMETERS	OLD PROTOCOL	MODIFIED PROTOCOL	p value
Number of Patients	n = 49	n = 31	
Mean age in years (range)	62.5 ±9 (37-86)	62.9 ±7 (51-82)	0.85
Gender			
Male (%)	33 (67)	23 (74)	0.62
Female (%)	16 (33)	8 (26)	
Mean Weight in kg (range)	86 ±21 (45-149)	86 ±22 (47 - 136)	0.94

Criteria	OLD PROTOCOL	MODIFIED PROTOCOL	p < 0.05	Phase/Standard
Liver enhancement (PVP)	51 ± 16 (n = 38)	61 ± 15 (n = 17)	✓	≥50 HU
Iodine concentration (mg I/kg)	456 ±112 (248-822)	595 ±88 (408-807)	✓	≥500 mg I/kg
Peak aorta (HAP)	242 ± 92	317 ± 98	✓	≥250 HU
Peak portal vein (HAP)	112 ± 41	180 ± 70	✓	"Avid"
Liver enhancement (HAP)	21 ± 12 (n = 38)	31 ± 15 (n = 17)	✓	20-30 HU
Peak hepatic vein (PVP)	144 ± 37	161 ± 32	✓	"Avid"
Liver enhancement (EP)	41 ± 15 (n = 27)	48 ± 10 (n = 17)	0.0521	Close to 50 HU

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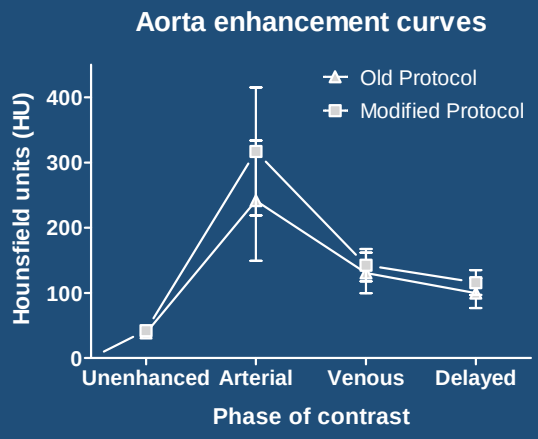
MEAN AORTIC ATTENUATION	Old Protocol	Modified Protocol	p value
Arterial phase	242 ± 92	317 ± 98	0.0008
Portal venous phase	131 ± 31	143 ± 25	0.08
Delayed phase	100 ± 23 (n = 38)	116 ± 19	0.003



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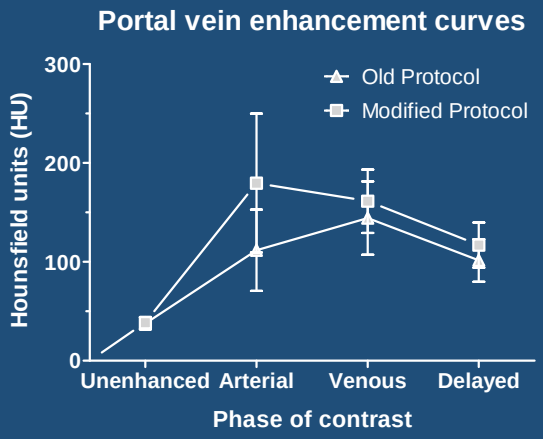
MEAN PORTAL VEIN ATTENUATION	Old Protocol	Modified Protocol	p value
Arterial phase	112 ± 41	180 ± 70	<0.0001
Portal venous phase	144 ± 37	161 ± 32	0.04
Delayed phase	102 ± 22 (n = 38)	117 ± 23	0.005



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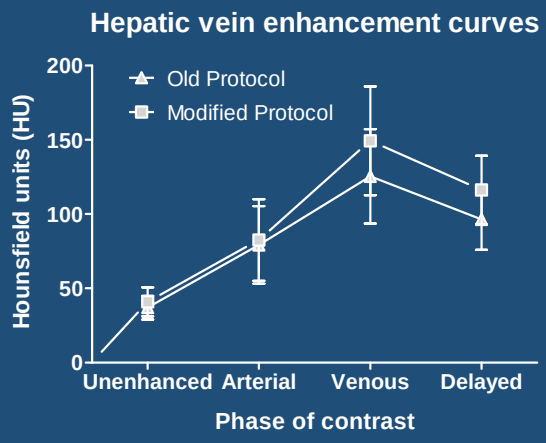
MEAN HEPATIC VEIN ATTENUATION	Old Protocol	Modified Protocol	p value
Arterial phase	79 ± 26	83 ± 27	0.59
Portal venous phase	125 ± 32	149 ± 37	0.003
Delayed phase	96 ± 20	116 ± 23	0.0003



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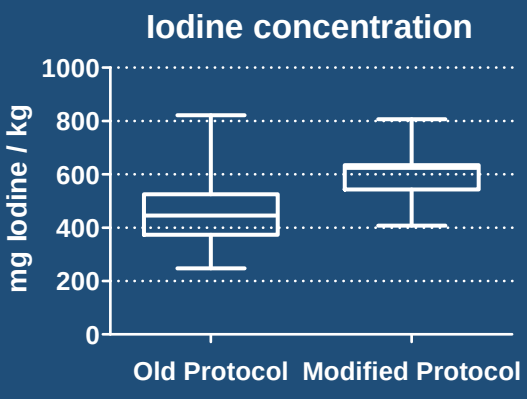
	Old Protocol	Modified Protocol	p value
Mean Iodine Concentration mg I/kg (range)	456 ±112 (248-822)	595 ±88 (408-807)	<0.0001



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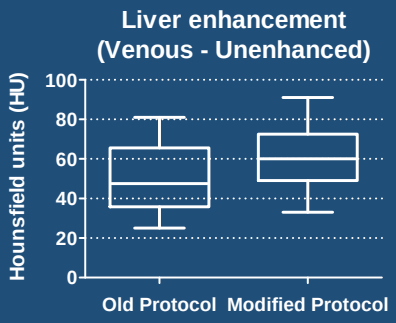
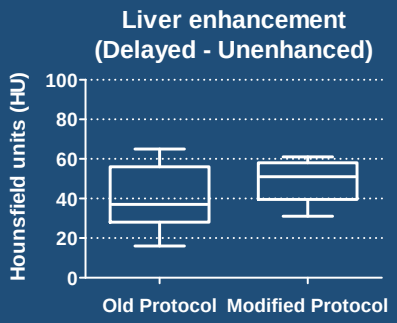
MEAN LIVER ENHANCEMENT	Old Protocol	Modified Protocol	p value
PVP - Unenhanced	51 ± 16 (n = 38)	61 ± 15 (n = 17)	0.0282
Delayed - Unenhanced	41 ± 15 (n = 27)	48 ± 10 (n = 17)	0.0521





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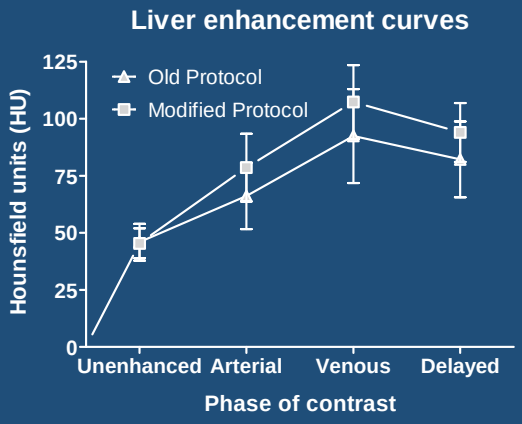
MEAN HEPATIC ATTENUATION	Old Protocol	Modified Protocol	p value
Unenhanced phase	46 ± 8 (n = 38)	46 ± 7 (n = 17)	0.95
Arterial phase	68 ± 13 (n = 49)	79 ± 14 (n = 31)	0.0006
Portal venous phase	95 ± 18 (n = 49)	108 ± 16 (n = 31)	0.002
Delayed phase	83 ± 16 (n = 38)	94 ± 13 (n = 31)	0.003



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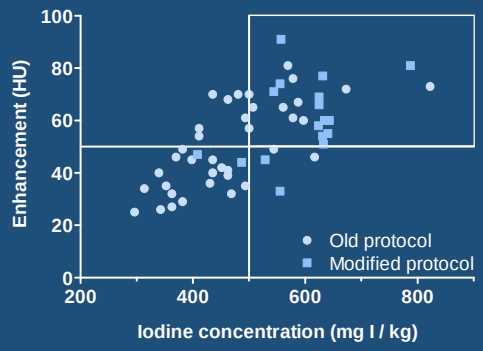
Iodine Concentration vs. Liver Enhancement



SUBOPTIMAL STUDIES	Old Protocol	Modified Protocol	p < 0.05
< 50 HU enhancement (PVP – unenhanced)	21 / 38	4 / 17	✓
< 500 mg I / kg (where unenhanced phase unavailable)	9 / 11	3 / 14	✓
Total suboptimal studies (%)	30 / 49 **(57%)**	7 / 31 **(23%)****	✓

ALL 7 SUBOPTIMAL STUDIES, PATIENTS >100kg

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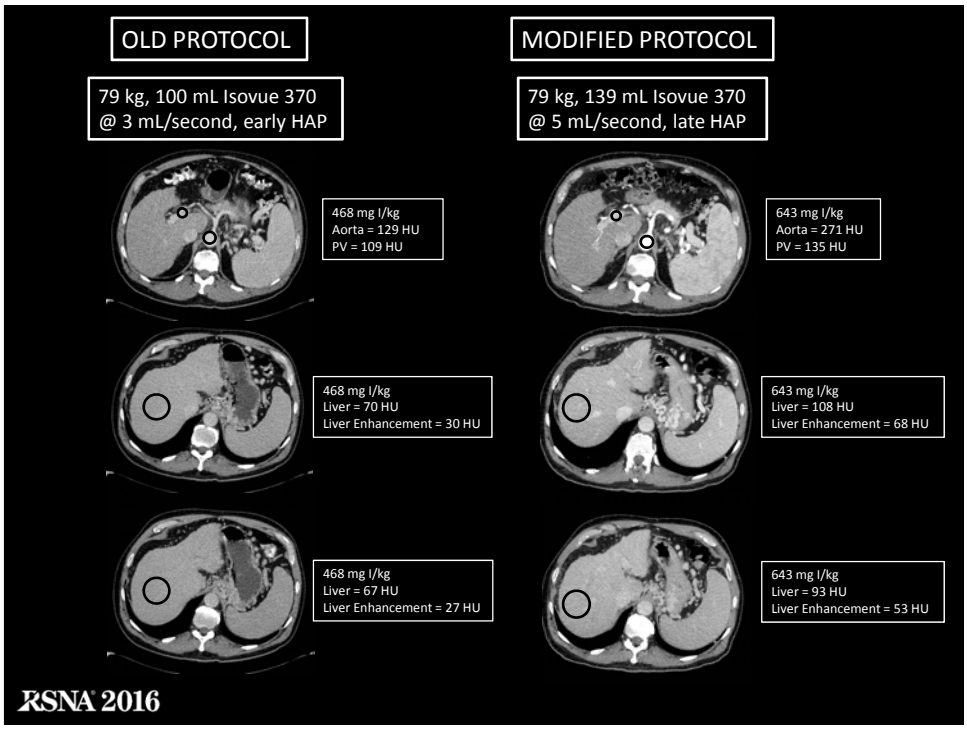

Discussion

- Addition to existing literature
- Contrast media pharmacokinetics
- Cost issues
- Future Directions
- Limitations

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Discussion: Addition to Literature

- To our knowledge, this is the first study to examine weight-based contrast dosing in a North American population of cirrhotic patients
- Majority of previous studies conducted in Asia, evaluated patients much smaller than the average North American
- The heaviest patients in these studies corresponded to the average weight of patients in our study

Study	Location	Number of Patients	Average Weight (kg)	Weight Range (kg)	Exclusion
Heiken et al., 1995 (Radiology)	Washington University	200	73	45-91	>95kg, cirrhosis
Yamashita et al., 2000 (Radiology)	Japan (3 university hospitals)	221	57	19-88	NO
Awai & Hori, 2003 (Eur Radiol)	Osaka, Japan	92	60	44-76	NO
Awai et al., 2004 (Radiology)	Osaka, Japan	199	57	35-83	NO
Sultana et al., 2007 (Radiology)	Kumamoto, Japan	192	60	34-81	NO
Kondo et al., 2008 (Radiology)	Gifu, Japan	161	56	37-75	>75kg
Yanaga et al., 2008 (AJR)	Kumamoto, Japan	135	59	34-85	NO
Kondo et al., 2009 (Radiology)	Gifu, Japan	120	52	30-80	cirrhosis
Li et al., 2010 (J Comput Assist Tomogr)	Emory University	77	79	50-112	NO
Fujigai et al., 2012 (Eur J Radiol)	Osaka, Japan	56	59	40-77	NO
Ichikawa et al., 2013 (Acad Radiol)	Japan (77 hospitals)	348	58	40-80	NO
Kidoh et al., 2013 (J Comput Assist Tomogr)	Kumamoto, Japan	100	55	27-88	NO
Kondo et al., 2013 (Eur Radiol)	Gifu, Japan	103	55	34-82	NO
Awai et al., 2015 (Radiology)	Japan (31 hospitals)	1288	58	29-110	NO
CURRENT STUDY	**Halifax, NS, Canada**	**80**	**86**	**45-149**	**NO**

Discussion: Contrast Media Pharmacokinetics

- Arterial enhancement is proportional to iodine administration rate
  - Increasing injection rate from 3 mL/s to 5 mL/s improved peak aortic attenuation
- Delaying the timing of the arterial phase resulted in increased opacification of the portal vein without changing the opacification of the hepatic veins
  - Corresponds with the ACR Li-RADS definition of a proper late arterial phase
- Hepatic enhancement is primarily determined by the volume of contrast administered
  - Main physiologic parameter affecting liver enhancement is body weight
  - By adjusting the dose of contrast media to patient weight, liver enhancement in the portal venous phase significantly improved and resulted in fewer suboptimal studies
  - All 7 suboptimal studies in the modified protocol occurred in patients weighing > 100kg who received the maximum contrast dose (150 mL) and therefore received a lower iodine concentration

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References 5-7,10-21,25-28

Discussion: Cost Issues

- Increased cost of IV contrast?
  - The modified protocol costs $5.60 (CDN) more per examination than the old protocol
  - At least partly offset by fewer repeat examinations due to inadequate/suboptimal studies, which decreased from 57% with the old protocol to 23% in the modified protocol
  - Decreased use of alternative, more expensive modalities such as MRI, which costs $50.97 (CDN) more than the modified protocol CT per examination
  - Better for patient care – HCC needs early detection for chance of survival

SUPPLIES	OLD CT	MODIFIED CT	MRI
Contrast (mL)	**100 @ $0.16/ml**	**135 @ $0.16/ml**	**12 @ $4.30/ml**
TOTAL CONTRAST (CDN$)	**16**	**21.60**	**51.60**
Equipment (needle, syringe, etc.)	9.31	9.31	9.31
Technologist	30 mins ($20.97)	30 mins ($20.97)	60 mins ($41.94)
Administrative costs	14.63	14.63	14.63
TOTAL COST (CDN$)	**60.91**	**66.51**	**117.48**

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Discussion: Future Directions

- Weight based dosing
  - In this audit, contrast dose was based on TOTAL body weight – may overdose obese patients as adipose is relatively less vascular
  - Other measures of body weight: lean body weight, body surface area, patient attenuation index, abdominal fat ratio may result in less overall IV contrast
  - In cirrhotic patients extra contrast may be required due to altered liver hemodynamics
- Reduce tube voltage
  - Decreasing kVp closer to K-edge of iodine results in less IV contrast needed
  - Studied in small patients with success
  - Issue in obese patients as artifacts from x-ray attenuation decrease image quality
  - Suggested unacceptable image quality cutoff occurs at >78.7 kg (average weight in our study was 86 kg)

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References 15-20, 32-45

Discussion: Limitations

- Single centre, partly retrospective
- kVp not constant between studies (automated CARE kV software on 2 of 3 scanners)
  - At lower kVp, the mean energy of the xray beam is brought closer to the k-edge of iodine
  - Lower energy xrays are absorbed to a greater degree by iodine-containing structures, resulting in higher attenuation values
- Unenhanced phase not always available (as not always required) to calculate enhancement
  - Iodine concentration used as surrogate
- Did not evaluate diagnostic accuracy of HCC detection
- Did not evaluate clinical outcomes

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Conclusions

- Modified protocol improved image quality in ALL phases
  - Increased injection rate = improved aortic attenuation
  - Late HAP = increased PV attenuation
  - Increased contrast volume = improved hepatic enhancement in both the PVP AND EP
- Number of suboptimal studies decreased from 57% to 23%
  - ALL patients in suboptimal group weighed >100kg - alternative strategy with MRI?
- Weight based contrast dosing, faster injection rate, and late HAP timing result in better quality studies in cirrhotic patients
  - Implication = better/earlier detection of HCC
- **Modified protocol being implemented across region**

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