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Long title: CT brain perfusion: a static phantom study of contrast-to-noise ratio and radiation dose

Short title: CTP contrast-to-noise ratio and radiation dose

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CT brain perfusion: a static phantom study of contrast-to-noise ratio and radiation dose

Abstract

Objectives: CT perfusion (CTP) is increasingly employed in the diagnosis and management of ischemic stroke but radiation dose can be significant and optimising contrast to noise ratio (CNR) is challenging. This study aimed to quantify and optimise the balance between CNR as a surrogate for image quality and radiation dose.

Methods: A perspex head phantom with vials of dilute contrast agent was scanned using a Siemens Definition Flash 128-slice scanner. The CTP protocol exposure parameters were adjusted over 70-120 kVp and 150-285 mAs. Measurements were obtained for the average dose per slice in Hounsfield Units (HU) for iodinated contrast agent, and the image noise for background regions of perspex. The CNR was measured as a function of the volumetric CT dose index (CTDIvol) and kVp.

Results: A change from 120 to 80 kVp, achieved the same CNR with 60% reduction in dose. Alternatively, for the same dose, the change from 120 to 80 kVp improved CNR by +58%. A change from 80 to 70 kVp whilst operating at the same CNR, led to 13% reduction in dose. Alternatively, maintaining the same dose while changing from 80 to 70 kVp improved the CNR by +7%.

Conclusion: Lower beam energies achieved the same CNR with less dose, or improved CNR at the same dose. A reduction from 80 kVp to 70 kVp may be clinically useful to optimise CTP acquisitions.

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keywords CT brain perfusion, contrast-to-noise ratio, radiation dose

Introduction

In suspected ischemic stroke, non-contrast CT brain may be normal in the first few hours after onset when potential reperfusion therapies are considered. CT perfusion (CTP) has the capacity to visualise the blood flow abnormality in ischemic stroke and therefore confirm the diagnosis as well as providing information about the severity of hypoperfusion and likely salvageability of brain tissue [1, 2]. The concept that patients with a large irreversibly injured region of brain, identified using CTP, are less likely to respond favourably to reperfusion was utilised in the selection criteria for two of the recent positive clinical trials of endovascular thrombectomy [3, 4]. CTP is incorporated in the routine imaging of ischemic stroke at some centres [5] but concerns are often raised regarding radiation dose [6] and contrast-to-noise ratio (CNR) can be limited as a result [7]. The acquisition involves repeated CT scanning of the brain during the passage of an intravenous bolus of iodinated contrast. The four dimensional data set is then processed to create statistical parametric maps (SPM) typically including cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT) and either time to peak (TTP) or time to maximum (Tmax) for ease of interpretation.

The scan protocol for CTP has evolved with advances in CT scanner technology. Very early CTP studies utilised the same scan parameters as CT brain studies operating at 120 kVp [8]. Faster detection systems have enabled dynamic studies at lower kVp, leading to the CTP scan protocol using 80 kVp to achieve reduced radiation dose to the patient and improved sensitivity to iodine based contrast agent [9]. Modern CT scanners with multiple rows of detectors are capable of rapid volume scanning, and advances in the X-ray source technology have now enabled two manufacturers to reduce their minimum beam energy from 80 to 70 kVp. Whilst lower energies deliver an improvement in radiographic contrast, the beam is less penetrating, so there is a reduction in the number of transmitted photons with an accompanying increase in noise. This loss of image quality can be offset by operating at higher mAs but at the cost of an increase in radiation dose to the patient.

Recent clinical studies have examined the influence on image quality and radiation dose offered by 70 kVp over higher energy spectra. Qualitative measures of image quality for brain angiography [10, 11] for 70 kVp over 120 kVp, found increased noise, increased CT numbers expressed in Housfield Units (HU), with similar image quality and significant dose saving (85% less). Comparison between 80 kVp with iterative reconstruction against 70 kVp with filtered backprojection (FBP) and different mAs for CTP achieved similar image quality at less dose and no significant differences in parametric maps [12]. For CTP at the same mAs, 70 kVp versus 80 kVp [13] uses 35% less dose, achieving similar image quality in parametric maps for CBF and CBV, with modest change in MTT for white matter.

This phantom based study aims to quantify the trade off between both image quality expressed as the CNR and radiation dose in the context of CTP. The absence of a suitable CTP phantom, prevents a dynamic study and subsequent analysis of SPM. Instead we focus on a single static frame to quantify radiographic contrast, image noise and patient dose metrics across a clinically relevant range of exposure settings kVp and mAs. The relationships between all parameters will be used to balance the trade-offs between CNR and radiation dose.

Materials and methods

The study was conducted using a Siemens Definition Flash 128-slice CT scanner (Siemens. Erlangen, Germany), with the CTP protocol technique factors summarised intable 1. The parameters chosen were centred around our clinical protocol utilising 80 kVp and 200 effective mAs (equal to the ratio of mAs to helical pitch), with a maximum mAs of 285 chosen as this was the system limit at 70 kVp. Whilst the Siemens flash scanner is Dual Source, during perfusion imaging it only uses a single source to operate as a conventional CT scanner, and acquires 30 temporal frames over 10 cm axial length reconstructed to 10x10 mm thick slices. Note that helical scanning involves over-beaming to collect an extra half rotation of data at the start and end of the scan [14], and this leads to the scanned volume being longer than the reconstructed volume. No dose modulation techniques were utilised and the system did not offer iterative reconstruction for CT perfusion.

The perspex CTDI head phantom (CIRS. Norfolk, USA) used is 16 cm diameter by 14 cm axial length with a physical density and composition approximating brain tissue. It was necessary to wrap the phantom with neoprene rubber (see figure 1) to suppress a strong cupping artefact arising from the skull attenuation correction employed by the CTP image reconstruction algorithm.

Vials of varying dilutions of iodine based contrast agent (table 2) were loaded into the five apertures contained within the perspex cylinder and the phantom scanned at four beam energies 70, 80, 100 and 120 kVp, each at three different exposures varying between 150-285 mAs. The five concentrations evaluated ranged between 1-10% to best mimic the *in vivo* situation, as radiographic contrast agent undergoes volumetric dilution to approximately 5% following IV injection and mixing with blood during a first pass through the heart and lungs [15].

The reconstructed data was exported to a workstation for quantitative region of interest (ROI) analysis with the open source tool box provided by ImageJ [16]. A circular ROI was drawn to enclose the contents of each vial excluding any air and the mean HU was used as a measure of radiographic contrast relative to the perspex background. A measure of image noise was obtained as the standard deviation for HU within a large circular ROI of perspex located midway between the centre and edge. Image quality was quantified using the contrast to noise ratio (CNR) as a figure of merit, evaluated as the ratio of mean HU for iodine to the standard deviation for nearby regions of perspex. Radiation dose is reported by the scanner as the volumetric CT dose index (CTDIvol) and is summarised in table 3. The effective dose in milliSieverts (mSv) was calculated using the CTExpo (V2.3.1) CT dose calculator [17] and modern tissue weighting factors [18].

Results

The mean HU for each iodine concentration established for each kVp are presented in figure 2, with error bars representing one standard deviation for the iodine ROI. The relationship between HU and iodine concentration is linear, up to a maximum available value of 3072 (as 12 bits are used to span the range -1024 to +3072), which translates to concentrations 96-180 mg/ml for the respective range 70-120 kVp.

Measured image noise is presented in figure 3 in units of HU. The curves shown were obtained by fitting to a polynomial function of the reciprocal of the square root of CTDIvol, assuming that Poisson counting statistics govern the detection system.

Measured CNR is presented as a function of CTDIvol in figure 4 for each iodine concentration, beam quality (kVp) and quantity (mAs). Non-linear regression analysis employed a Marquardt-Levenberg algorithm, to fit curves [19] to the measured CNR at each kVp against the square root of CTDI, and weighted by the reciprocal of HN uncertainties of 2-10% presented in figure 3. As detailed statistical analysis was not required, we did not use the 1-3% uncertainties (ratio of one standard deviation to the mean) for the fitted coefficients.

Tables 4 and 5 show changes in dose and CNR required to maintain the same CNR and dose respectively relative to variations in kVp from the clinical protocol of 80 kVp and 200 mAs. The fitted curves were used to draw the horizontal and vertical arrows joining different kVp results. For the same CNR, lower kVp delivers less dose; -39% (120 to 80 kVp), -42% (100 to 80 kVp) and -13% (80 to 70 kVp). For the same dose, lower energies achieve better CNR: +58% (120 to 80 kVp), +32% (100 to 80 kVp) and +7% (80 to 70 kVp).

Table 6 summarises the calculation steps for estimating effective dose (E) based upon exposure factors required to achieve the same CNR at each kVp. The clinical protocol (table 1) was scaled to estimate CTDIvol using results in table 4, with effective mAs estimated using table 3, DLP calculated for 10 cm scan length repeated over 30 temporal frames and effective dose was calculated as described in the materials and methods.

Discussion

The detection task for CTP is to resolve small changes in HU due to the presence or absence of iodinated contrast agent in minute blood vessels within the brain, from the background image noise. For CTP, each volume scan is repeated over multiple temporal frames, so there is a need to optimise the trade off between CNR and radiation dose.

Our phantom based measurements quantify how the radiographic contrast improves at lower kVp. Figure 2 shows 50% improvement in contrast by changing from 120 to 80 kVp and a further 20% improvement by changing 80 to 70 kVp. Lower kVp is also accompanied by a reduction in dose with a subsequent increase in background noise due to there being fewer transmitted photons (see Figure 3).

Our findings in Figure 4 show that using our current clinical CTP scan protocol (80 kVp, 200 mAs and CTDIvol of 8.5 mGy) as a comparator to achieve the same CNR (and presumed clinical diagnostic utility) at 70 kVp a dose saving of 13% is achieved. Whilst this is a relatively small improvement, for a CTP protocol with scan length of 10 cm with 30 temporal frames we estimate the total effective dose saving in moving to a 70 kVp CTP protocol is about 0.6 mSv. Our results also show that performing CTP at 100 to 120 kVp results in unacceptably high patient doses of 10.4 to 14.6 mSv in achieving the same CNR as for 80 kVp. Similar changes in dose for the same CNR (horizontal displacements in figure 4) are reported in recent clinical and phantom based studies [10-11] for the CT angiography protocol. Clinical CTP using the same mAs for reduced kVp [13], is represented in figure 4 as the diagonal shifts between kVp curves to reduced dose and CNR. These trends are due to there being fewer photons in the transmitted spectrum leading to reduced dose and increased noise. When changing 80 kVp to 70 kVp, even fewer photons are available because the K-edge for a Tungsten anode is 69.5 keV so characteristic x-ray production is almost absent. Alternately (if clinically desired), in moving from an 80 to a 70 kVp CTP protocol whilst maintaining the same radiation exposure, (vertical displacement in figure 4) provides a 7% improvement in CNR. Statistical parametric analysis delivers quantitative information about dynamic flow parameters, which are not available from our static phantom study. We would anticipate improved CNR to deliver SPM with similar mean values and reduced uncertainty (i.e., less noise).

It should be noted that the results in this study are not unexpected on the basis of well established radiation physics models [14, 20], but they do provide experimental evidence that they may be applicable to the clinical scenario of brain CTP given the phantom we used. An assumption in the study design is that the concentration of intra arterial iodinated contrast within microvasculature (not ever evaluated as far as we are aware) mirrors that as established in larger central vessels (average of 5%). In addition, we also assume that the image noise for regions of brain tissue is similar to that for regions of perspex. We believe these are reasonable assumptions.

Our measurements considered typical in vivo arterial concentrations of contrast agent with relative dilution of 0.9-9%. In the theoretical scenario where mAs could be adjusted such that CT scans at 70 and 120 kVp achieved the same CNR we would expect the diagnostic outcome to be similar as these images are utilized to calculate change over time (eg.

Blood flow). The absolute numbers generated are not relevant, as these images are not used for diagnostic purposes in their own right (the individual images generated in clinical CTP are purposely as low dose as possible and hence are considered ‘non diagnostic’). CT perfusion aims to detect small changes in blood flow in the brain parenchyma in order to accurately assess cerebral blood flow and the other perfusion parameters. Increased image noise reduces the ability to detect these changes as the tissue enhancement in white matter may be only a few HU. The criteria for visibility [14, 20] is a CNR greater than 5, which is approached at lower concentrations and low doses. Extrapolation of the results in figure 4 (c) and (d) suggest such a limit is reached at 70-80 kVp for approximately 0.5% relative dilution and 5 mGy CTDIvol. The CNR for microvasculature in vivo might be reduced due to partial volume effects. Strategies for improving the CNR include increasing the iodine delivery rate (by raising one or both of the iodinated contrast concentration or the rate of intravenous injection), and/or reducing the image noise by temporal filtering and using iterative reconstruction over filtered back projection (not an option on our scanner for perfusion CT at the time of the study).

Conclusions

Our head phantom based measurements have demonstrated that changing the CTP protocol from 80 to 70 kVp can deliver a 13% dose reduction (for the same CNR) or a 7% improvement in CNR (for the same dose). We believe these results can be used to justify an in vivo investigation of CTP at 70 kVp rather than the currently used value of 80 kVp.

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Table 1 Exposure parameters for the clinical CTP protocol at the time of the study.

Scan length (mm)	118
kVp selected	70, 80, 100, 120
Gantry rotation (s)	0.285
Helical pitch, P	0.5
Effective mAs	150, 200, 285
Dose modulation	OFF
Collimation x Pitch (mm)	128 x 0.6 x 0.5= 38.4
Reconstruction filter	H20f
Reconstructed voxel side (mm)	0.39
Reconstructed slice thickness (mm)	10
Reconstruction volume axial length (mm)	100

Table 2 Measured mass density ρ and estimates for iodine concentrations.

Dilution (%)	**ρ (g/cm^3)**	**Iodine (mg/ml)**
100	1.402	350
8.7	1.015	30.5
7.1	1.012	25
3.9	1.005	13.5
1.9	1.000	6.6
0.94	0.994	3.3

Table 3 CTDIvol reported by the scanner as a function of kVp and effective mAs

Effective mAs	**CTDIvol (mGy)**			
	70	80	100	120
150	4.13	6.35	12.3	19.5
200	5.40	8.46	16.4	26.0

285	7.84	12.1	23.4	37.1

Table 4 Relative change in CTDIvol for fixed CNR and variable kVp.

I (mg/ml)	**70 to 80 kVp**	**90 to 100 kVp**	**100 to 120 kVp**
30.5	1.14	1.71	2.50
25.0	1.16	1.66	2.38
13.5	1.16	1.68	2.27
6.6	1.14	1.68	2.27
3.3	1.18	1.98	3.13
mean	**1.15**	**1.74**	**2.50**

Table 5 Relative CNR change, for fixed CTDIvol and variable kVp.

I (mg/ml)	70 to 80 kVp	80 to 100 kVp	100 to 120 kVp
30.5	1.06	0.76	0.63
25.0	1.06	0.78	0.65
13.5	1.07	0.77	0.66
6.6	1.07	0.77	0.66
3.3	1.08	0.79	0.56
mean	**1.07**	**0.77**	**0.63**

Table 6 Estimation of effective dose (E) at each kVp for 30 frames, 10 cm scan length and same CNR**.**

kVp	**70**	**80**	**100**	**120**
Effective mAs	270	200	180	160
CTDIvol (mGy)	7.4	8.5	14.8	21.3
DLP (mGycm)	2230	2540	4440	6240
E (mSv)	5.3	5.9	10.4	14.6

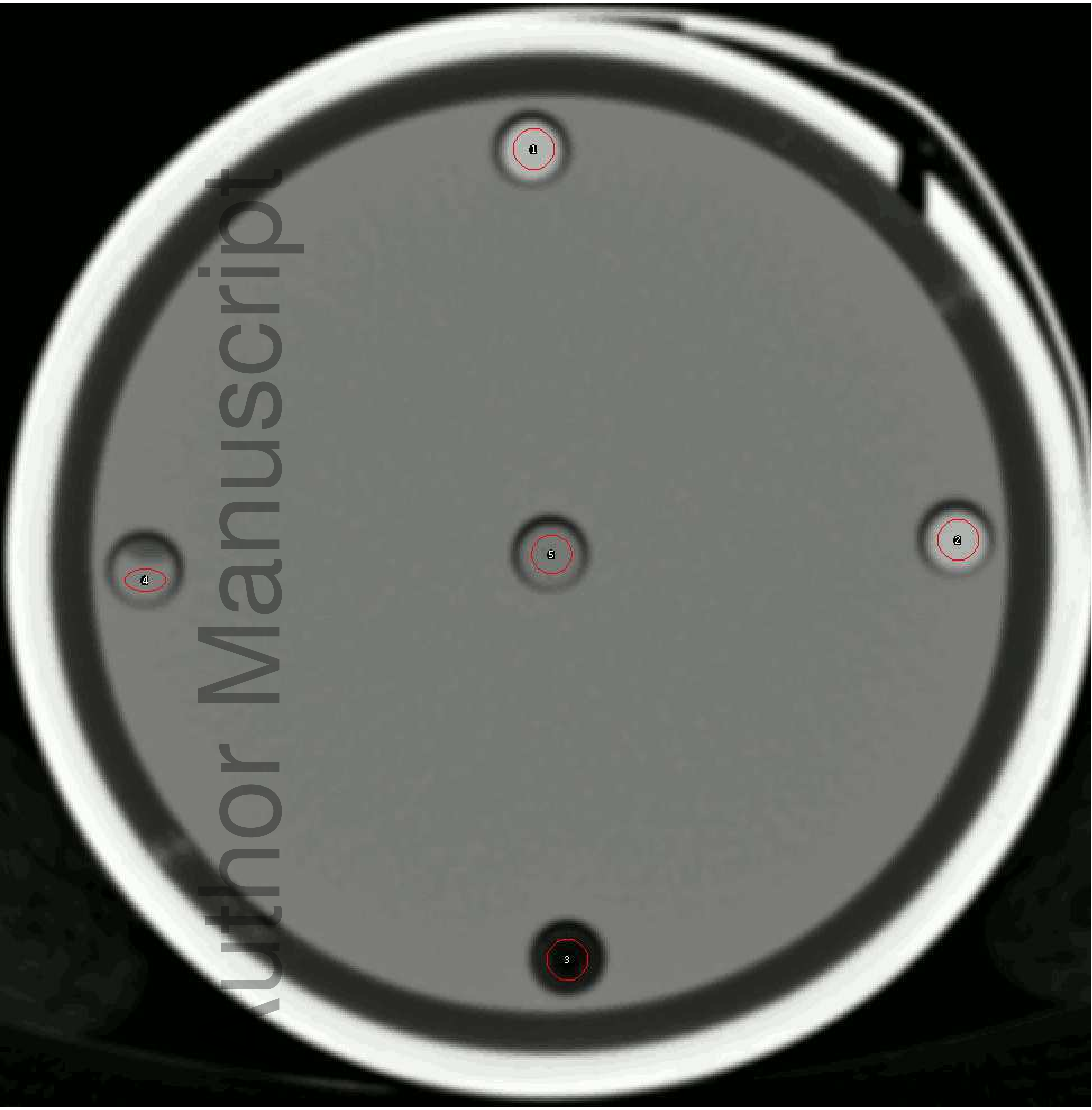
Figure 1 The CTDI head phantom wrapped with neoprene rubber, showing vials of dilute contrast agent inserted into the five aperture. Regions of interest (red) enclose the vial contents avoiding any trapped air (9 o'clock) whilst the 6 o'clock vial is in an adjacent slice.

Figure 2 Measured HU as a function of iodine concentration and kVp,

Figure 3 Image noise in regions of perspex as a function of the radiation dose per slice (CTDIvol), kVp (lines) and mAs (points), with the filled black circle denoting the CTP protocol used for this study.

Figure 4 CNR as a function of radiation dose, kVp (curves) and mAs (points) for (a) 25 mg/ml (7.1%), (b) 13.5 mg/ml (3.9%), (c) 6.6 mg/ml (1.9%) and (d) 3.3 mg/ml (0.9%). Error bars denote one standard deviation for each iodine ROI. A filled black circle identifies the CTP scan protocol used in this study (80 kVp and 200 mAs for 8.5 mGy). The vertical and horizontal arrows denote CNR for the same dose and dose for the same CNR respectively.

end



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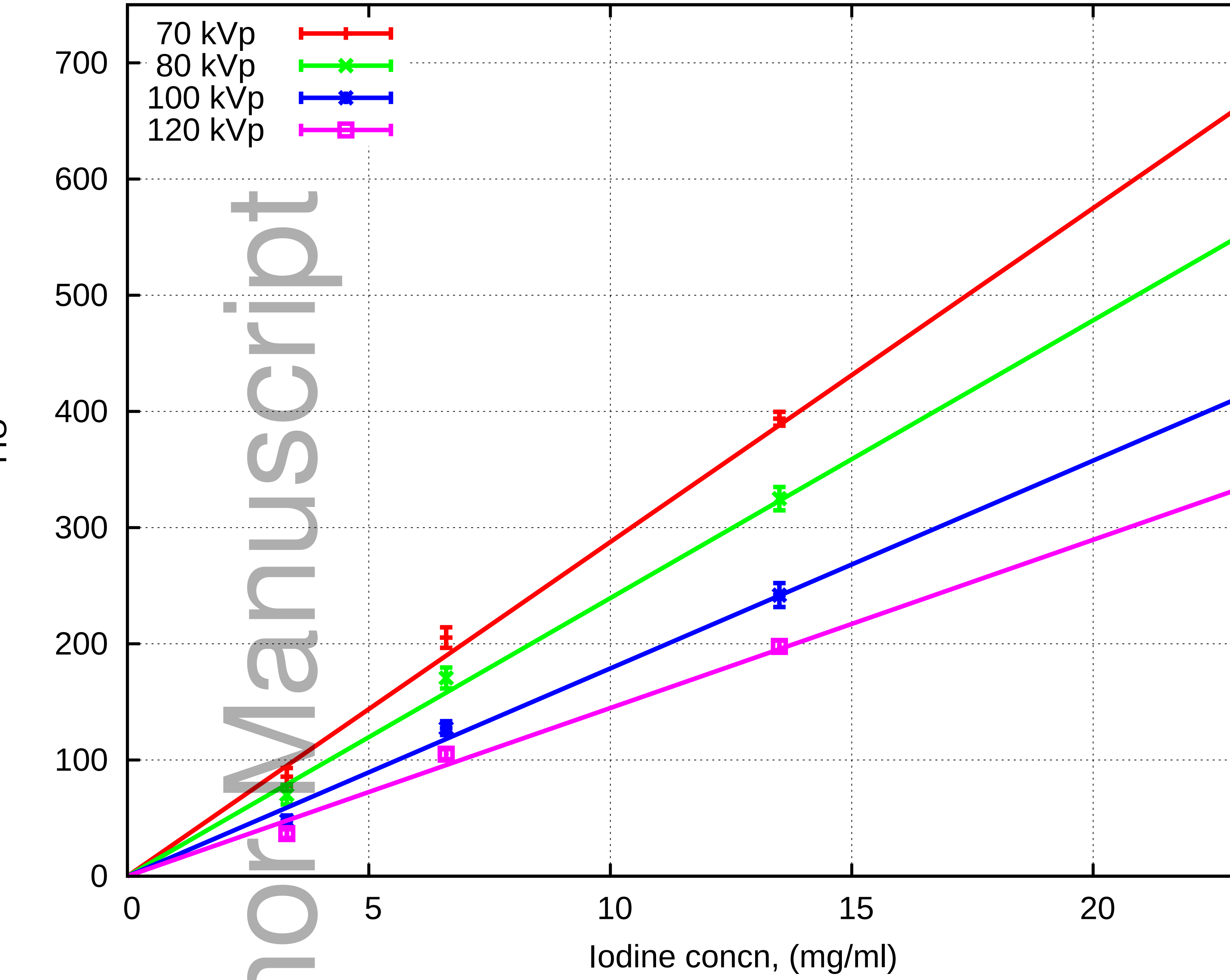

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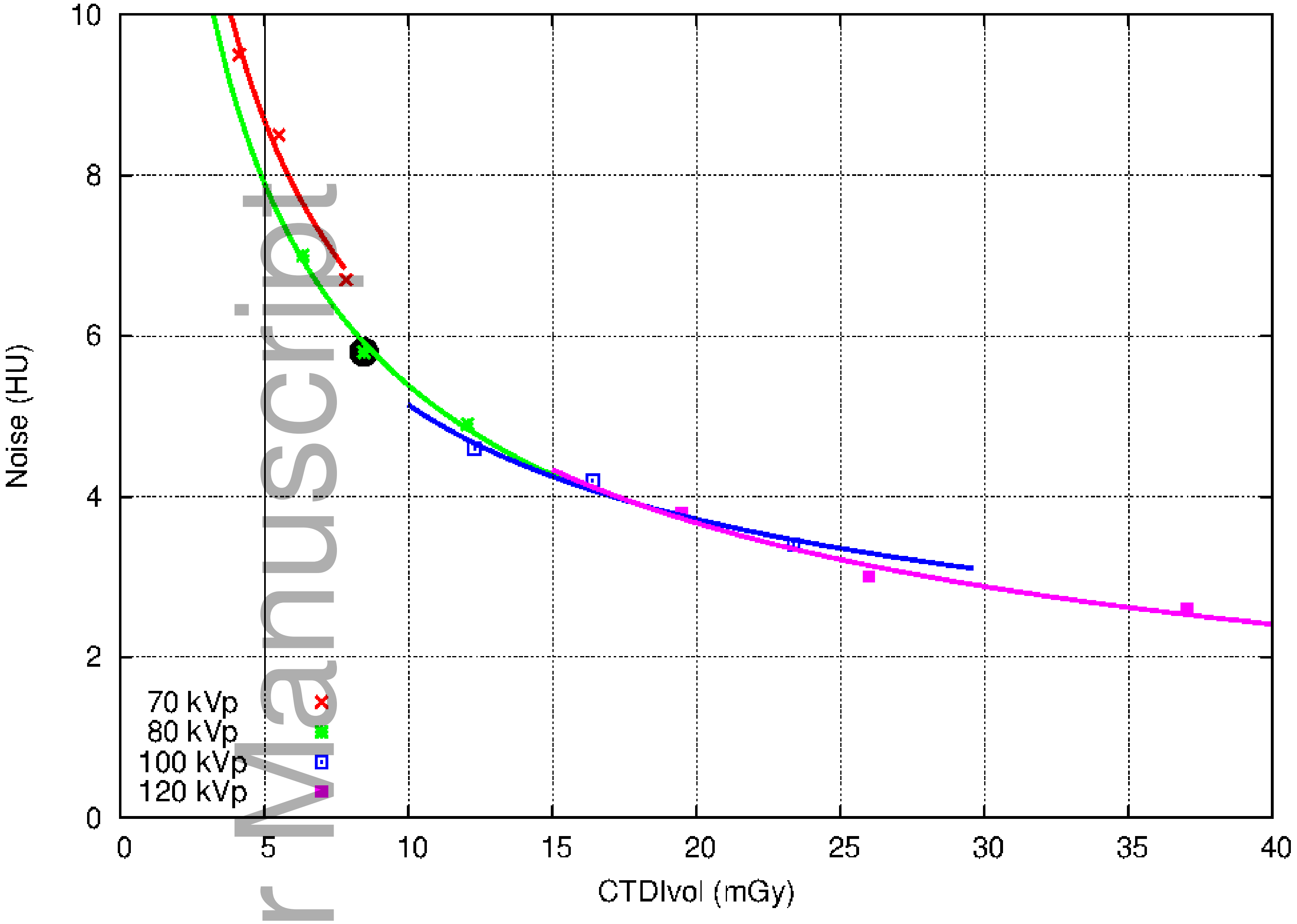

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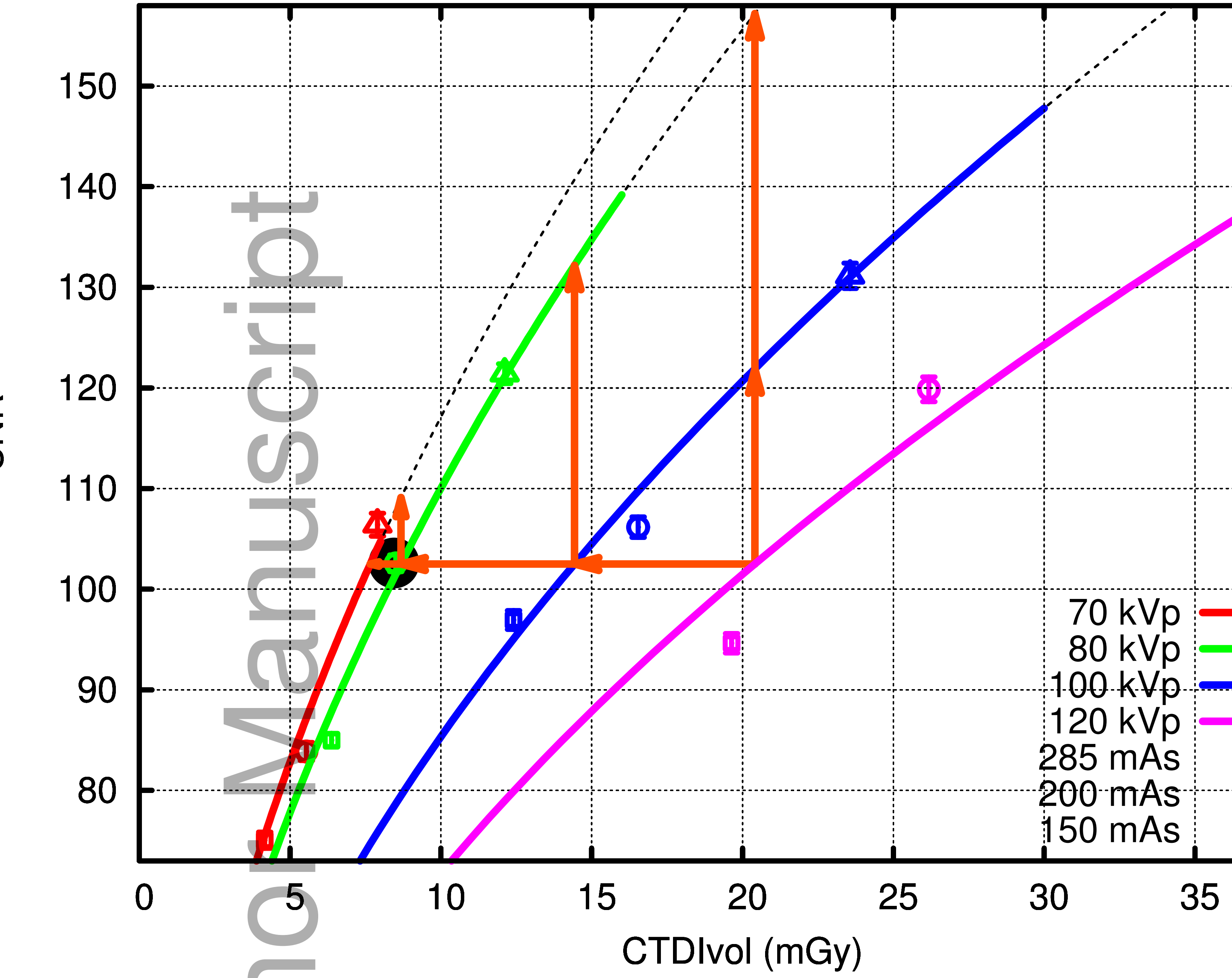

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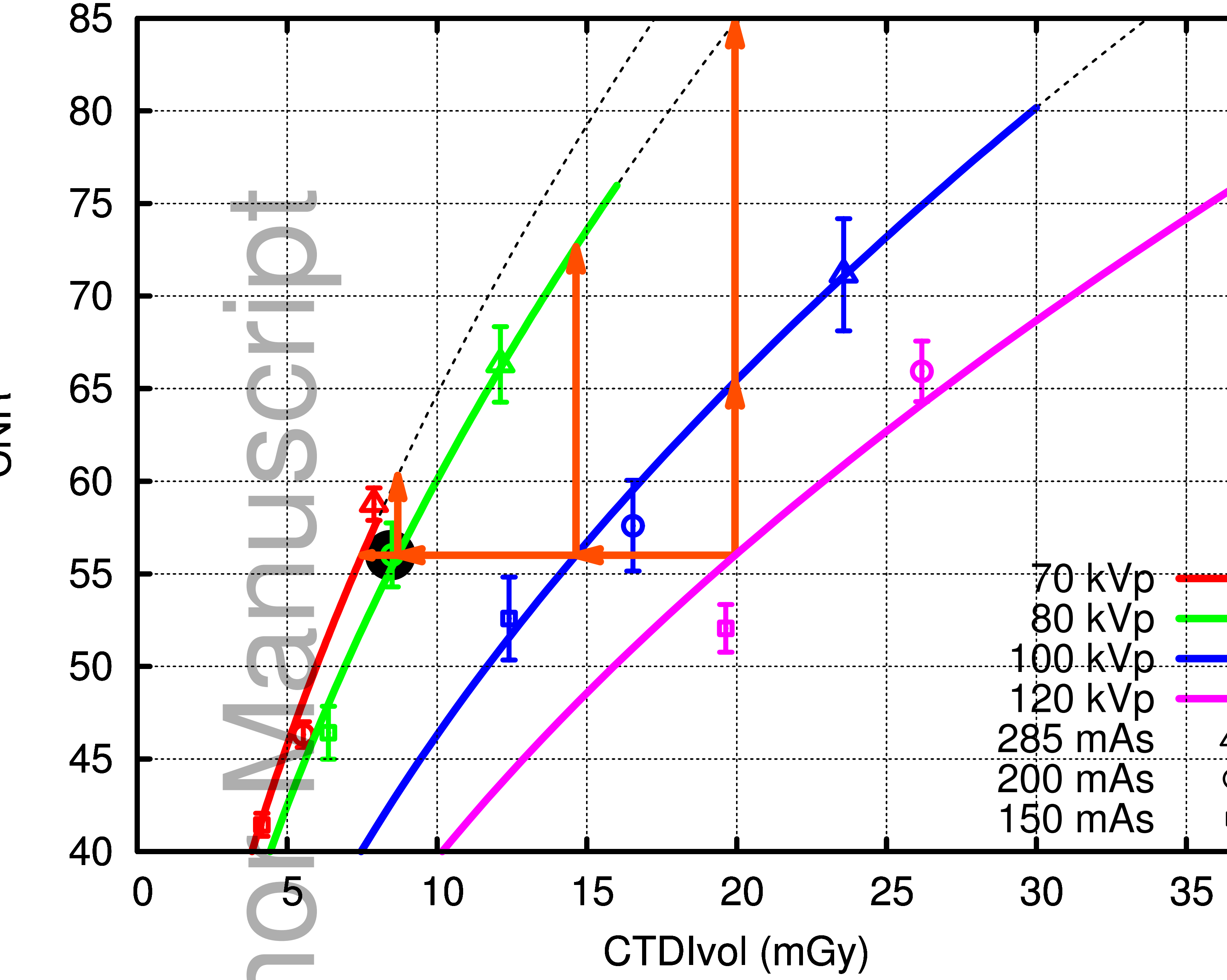

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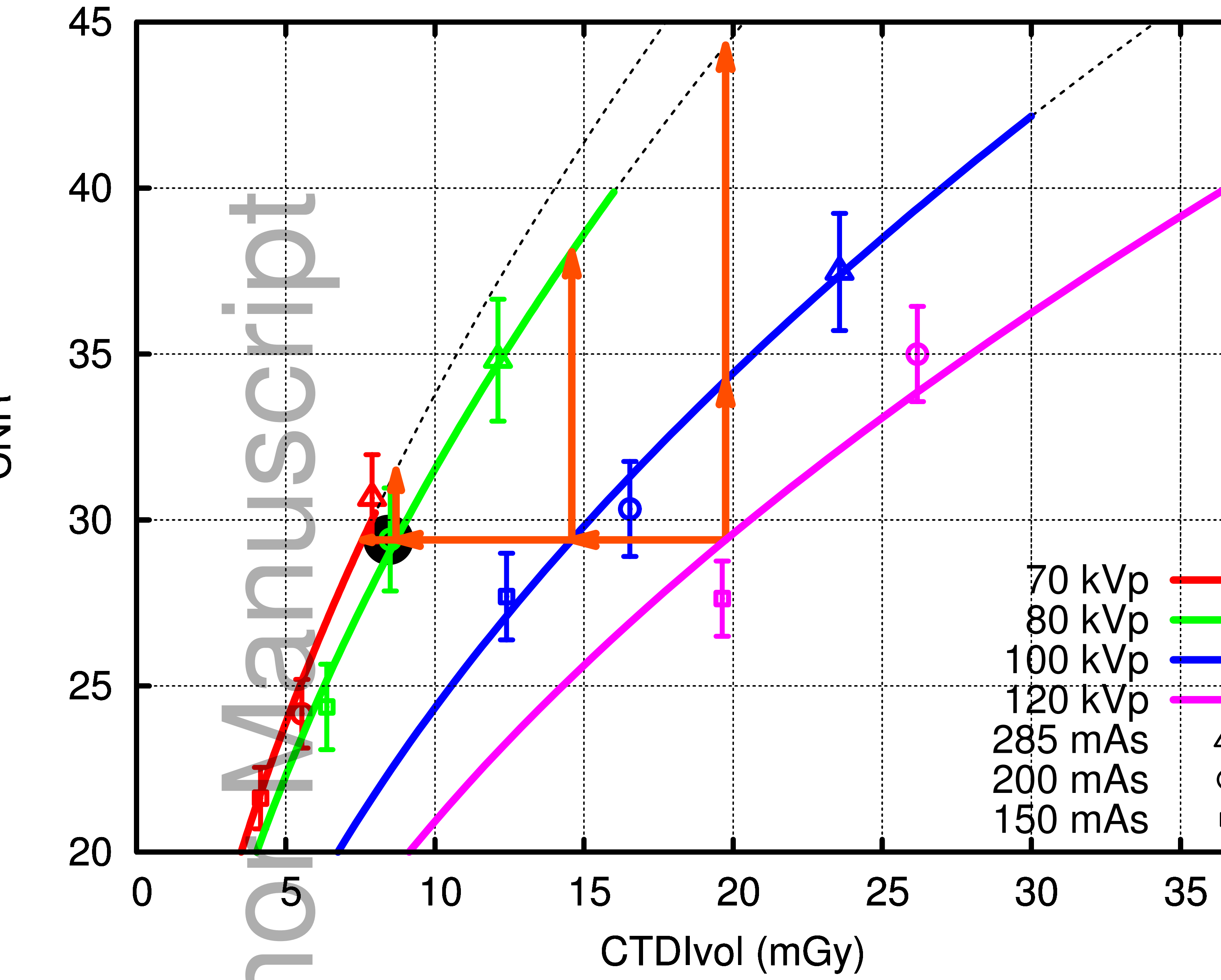

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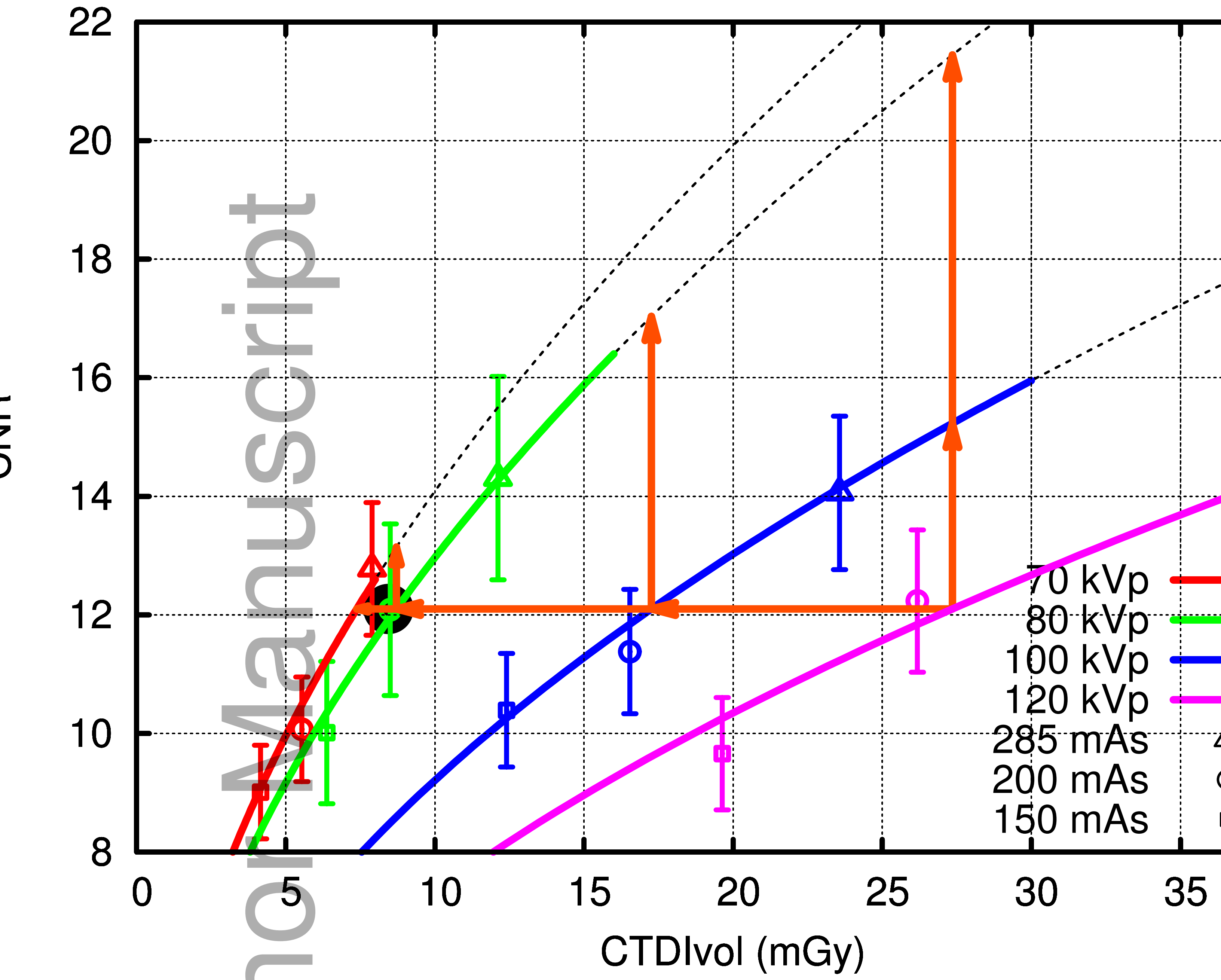

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