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CT and MRI-based Door-Needle-Times for acute stroke patients

A quasi-randomized clinical trial

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Abstract:

Objectives:

Door-Needle-times (DNT) of 20 minutes are feasible when Computer Tomography (CT) is used for first-line brain-imaging to assess stroke-patients' eligibility for intravenous-tissue-Plasminogen-Activator (iv-tPA), but the more time-consuming Magnetic Resonance Imaging (MRI)-based-evaluation is superior in detecting acute ischaemia.

The aim of this study was to compare DNT for CT versus MRI-based acute stroke-evaluation.

Patients and Methods:

Consecutive acute stroke-patients admitted to an acute stroke-unit were quasi-randomized to CT or MRI-based assessment and treated with iv-tPA, if eligible.

Door-Decision-Time and DNT for CT versus MRI-examined patients were compared and predictors of treatment-delay identified.

The effect of using MRI as the primary imaging-strategy upon the modified-Rankin-Scale (mRS) at three months was assessed using the validated electronic COMPASS-tool.

Results:

Four-hundred-forty-four patients were included. Median DNT in CT-allocated patients (22 (IQR 16) min) was significantly shorter than in MRI-allocated patients (30 (IQR 14) min), $p=0.005$.

The COMPASS-tool predicted that chance of independent living (mRS<3) at 3 months decreased with 1% in 16.9% of iv-tPA-treated MRI-examined patients due to the median treatment-delay of 8 minutes. In MRI-allocated patients; MRI were not feasible in 23.7% due to contraindications, in

16.1% due to clinical conditions and in 6.8% due to organizational issues. 16.8% of CT-allocated patients (pregnant/<30 years) received MRI to avoid X-ray irradiation or due to doubtful clinical presentation of stroke requiring MRI confirmation prior to receiving tPA.

Conclusions:

CT-based acute stroke evaluation is significantly shorter more feasible than MRI-based evaluation and potentially translates into time-related superior long-term outcome. However, the clinical impact is not detectable.

Introduction:

The ideal primary radiological image-modality used for evaluation of patients with symptoms of acute stroke prior to administration of intravenous-tissue-Plasminogen-Activator (iv-tPA) must be: Of diagnostic quality, short duration to diminish treatment-delay, feasible in the majority of patients and suitable for examination of restless, claustrophobic or critically ill patients. The ability to safely exclude intracerebral hemorrhage and stroke-mimicking pathologies contraindicating iv-tPA is further imperative. Demonstration of early signs of ischemia is not an indispensable requirement but is helpful in patients with atypical clinical presentations.

The pros and cons of Computer-Tomography (CT) versus Magnetic-Resonance-Imaging (MRI) to evaluate patients with symptoms of acute stroke prior to intravenous-tissue-Plasminogen-Activator (iv-tPA) treatment have been widely debated. CT-based Door-to-Needle-Times (DNT) of 20 minutes have been proven feasible (1) motivated by time-dependent efficacy of iv-tPA, but the more time-consuming MRI-based evaluation may provide additional information about hyper-acute cerebral ischemia (2) and iv-tPA-contraindicating stroke-mimicking pathology.

To answer the question if CT or MRI is the optimal imaging-strategy in the evaluation of patients with symptoms of acute stroke, a single-center quasi-randomized clinical-trial was conducted to compare several aspects of CT and MRI-based acute stroke-evaluation prior to administration of iv-tPA.

The aim of this preplanned sub-study was to compare DNT and perform a simulated prediction of the difference in long-term outcome between CT and MRI-examined patients.

Patients and Methods:

This quasi-randomized clinical-trial included all consecutive patients (>17 years of age) admitted with symptoms of acute stroke within 4.5 hours from symptom-onset to a single hyper-acute stroke-unit, on even weekdays from 8a.m. to 3p.m., from December 2013 to November 2015. All patients from the Region of Copenhagen (1.7 million) are referred directly to our institution on even dates and to another University-hospital on uneven dates.

In summary, all patients were by the emergency-service directly brought to a dedicated stroke-room within the Department of Radiology and were then evaluated according to a fast-track set-up. The patients were met by a pre-notified stroke-team; comprising a neurologist, a stroke-nurse, a neuro-radiologist, two radiographers and an orderly. The team members worked simultaneously, each with well-defined allocated tasks.

The neurologist was a senior-stroke-neurological-consultant (n=6, seeing 74.5% of the patients), a certified neurologist (n=4, seeing 12.8% of the patients) or a neurological-resident in the final six month of training prior to full neurological certification under telephone-supervision of a senior-stroke-neurological-consultant (n=14, seeing 12.6% of the patients).

If eligible, patients were treated with iv-tPA and if appropriate with endovascular therapy after the allocated imaging had been performed.

Randomization and imaging:

All patients were quasi-randomized to receive CT or MRI according to an equal number of predefined CT and MRI-days that were stated in calendar posted in the Department of Radiology well in advance.

In a quasi-randomized trial, patients are systematically allocated according to a predefined system (such as alternation, date of birth, case record number or as in our case according to admission date).

All patients were systematically assessed according to a Standard-Operational-Plan (SOP) for undertaking CT and MR imaging. The SOP was strictly followed in accordance with allocation but allowed for predefined cross-over between the CT and MRI in case of contraindications or vital medical needs for MR or CT such as: suspicion of intracerebral malignancy; MRI incompatible implants; lack of reliable information about MRI contraindications; too large body size; severe illness or restlessness that MRI was not safe; pregnant; less than 30 years of age. MRI-safety was adhered to according to International Guidelines.

On CT-days, a non-contrast-CT of cerebrum (scan-time 17.3 seconds) was conducted followed by a CT-angiography (scan-time 31.6 seconds) if no contraindications, preferably after administration of the iv-tPA-bolus.

On MRI-days, patients had DWI, Flair and Gradient sequences (scan-time 6.4 minutes) followed by a Time of Flight-(TOF)-angiography (scan-time 7.0 minutes), preferably after administration of the iv-tPA-bolus.

If the iv-tPA was administered before the angiography, the angiography was conducted immediately after administration of the tPA-bolus and thus no later than two minutes after the initiation of the tPA-therapy. The patient remained on the scanner bed throughout image conduction and administration of the tPA.

The neuro-radiologist planned the image-conduction in collaboration with the CT and MRI-technicians when pre-notified of an incoming patient. No patients were allowed to wait for more than 10 minutes for the allocated imaging to be performed; if the radiological staff foresaw that the allocated image-modality would not be available in time, a cross-over was arranged to avoid treatment-delays in accordance with the SOP.

The imaging was assessed by a neuro-radiologist who read the imaging directly in the control-room before passing on the conclusion to the stroke-physician.

On MRI-days three 20 minutes time-slots were reserved for the trial; when acute MRI-allocated stroke-patients arrived, the MRI-technicians were as a consequence able to catch-up on the preplanned MRI-examinations and thus fully exploit the MRI-capacity.

Sample size:

As no preceding equivalent trials have been conducted, sample-size was estimated based on an anticipated difference in DNT of MRI and CT-based assessment. With a least clinically relevant difference of 10 minutes, SD at 20 minutes, α -two-tailed at 0.05 and β at 90%, the total number of participants was estimated at 172 patients. The sample-size was extended in order to allow for secondary outcomes not reported in this sub-study.

MRI-safety:

On MRI-days, MRI-safety-procedures were strictly adhered to. To reduce the time taken to complete the safety-procedures an MRI-radiographer was present when the neurologist completed the MRI-safety-checklist rather than duplicating the procedure in the MRI-suite. Outside the MRI-room, a short time-out was imposed to ensure that the MRI-safety-checklist had been reviewed and loose metal-objects removed from both patient and staff-members entering the MRI-room.

A pilot-period of two weeks preceded the trial to ensure high efficiency and staff-awareness in regard to the new time-saving MRI-safety-routines.

Time-registration:

To ensure a consistent time-registration, intervals from admission to treatment-decision (Door-Decision-Time (DDT)) and to administration of the iv-tPA-bolus (DNT) were recorded systematically.

Symptom-onset was defined as witnessed stroke-symptom-onset or when the patient was last seen well. Admission was defined as when the patient entered the dedicated stroke-room at

which point the stroke-nurse finalized the electronic patient-registration. Time from arrival of the ambulance to the patient entered the stroke-room was less than one minute.

The time of the treatment-decision was defined as when the stroke-physician decided to prescribe or refrain from prescribing iv-tPA-treatment.

Time of iv-tPA-administration is a mandatory part of the stroke-patient-file from which the time of iv-tPA-administration was later extracted.

The number of patients evaluated during a shift (by the same stroke-physician) and 20-minute time-intervals between arrivals of patients were calculated.

Outcomes:

National Institute of Health Stroke Scale (NIHSS) and pre-onset modified Rankin Scale (pre-mRS) were on admission established by the stroke-physician.

As part of the institutional follow-up, the iv-tPA-treated patients were by telephone contacted by an outpatient-nurse who recorded the mRS at three months.

The COMPuterised decision Aid for Stroke thrombolysis (COMPASS)-app (3, 4) is validated for prediction of the risk of iv-tPA-induced Symptomatic-Intracerebral-Hemorrhage (SICH) according to the SITS-MOST-definition, mortality, independent living (mRS <3) and dependent living (mRS 3-5) at three months after iv-tPA treatment. The app gives the risk (in percent) of each of the four outcomes based on entering of the patient's individual risk profile; age, gender, diabetes, previous stroke, presence of recent infarct on CT or MRI, daily use of aspirin/clopidogrel, time from onset to iv-tPA-treatment (ONT), glucose-concentration, systolic blood-pressure and NIHSS.

We used the COMPASS-app to predict the four outcome-measures for each individual iv-tPA-treated MRI-allocated patient in different two scenarios; 1, the actual scenario where the patient is admitted on an MRI-day (imitating admission to a primary MRI-based stroke center) 2, a theoretic scenario where the patient instead is admitted on a CT-day (imitating admission to a primarily CT-based stroke center). The two predictions were based on entering of the true individual ONT and the true ONT subtracted the median difference in ONT between MRI and CT-allocated patients respectively (the treatment-delay caused by MRI compared to CT-based assessment). All other predictors remained fixed. The four outcomes were thus predicted twice for each patient; an individual prediction illustrating admission on an MRI versus a CT-day respectively. The predicted four paired outcomes were compared for each iv-tPA-treated MRI-allocated patient.

Statistical analysis:

Continuous data were compared with students-t-test and non-parametric continuous data with Mann-Whitney-U-test. Categorical data were compared with Chi-square-tests.

Two random-effects-models allowing for the cluster-effect of the stroke-physicians each seeing more than one patient were constructed to identify predictors of DDT and DNT, the latter only for iv-tPA-treated patients. The following variables were tested as predictors of DDT and DNT in both

models; age, gender, conducted image-modality, crossover from allocated scan, NIHSS, stroke-physician-seniority, time to arrival of the next patient (20-minute intervals) and the numbers of patients evaluated during the shift by the same stroke-physician. Discharge-diagnosis (ischemic stroke, Intracerebral Hemorrhage, TIA or stroke-mimicking-diagnosis), pre-onset mRS, and if thrombolysis was prescribed were furthermore added to the model testing predictors of DDT. DDT and DNT were log-transformed to comply with test-assumptions. The presented estimates, Standard-Errors and 95% Confidence-Intervals (CI) (table 7+8) were back-transformed.

To check for a learning-effect on DNT, DNT were tested with simple linear-regression as function of the consecutive patient-IDs to assess for systematic changes in DNT as consequence of gained experience among the stroke-team-members and institutional use of hyper-acute MRI.

mRS at three months for CT versus MRI-allocated iv-PA-treated patients were compared with ANCOVA adjusted for the pre-onset mRS.

Due to cases of cross-over between image-modalities, data are presented according to allocation (intention-to-treat) as well as according to the image-modality performed (per-protocol).

Statistical analyses were conducted using SAS-Enterprise (Version 7.11, Cary, NC, USA) and IBM SPSS-Statistics (Version 20.0, IBM Corp, Armonk, NY, USA).

The trial was approved by the Copenhagen-Regional-Ethics-Committee (H-4-2013-118) and the Danish Data-Protection-Agency (2007-58-0015) and registered at ClinicalTrials.gov (NCT02780843).

Results:

Four-hundred-forty-four consecutive patients presenting with symptoms of acute stroke within 4.5 hours from symptoms-onset were included into this study (fig 1). Two-hundred-twenty-five patients were quasi-randomized for CT and 219 for MRI.

Due to contraindications or when it was not possible to be sure about MRI-contraindications, cross-overs to CT-assessment were done in 52 (23.7%) MRI-allocated patients (table 1). In addition there was cross over for 40 (16.1%) MRI-allocated patients due to clinical conditions which required a CT-assessment and further 15 (6.8%) patients due to organizational issues. Twenty-two (9.8%) out of 225 CT-allocated patients received a MRI head scan: to avoid X-ray irradiation in a pregnant patient; 5 patients were <30 years; and further 16 patients had a doubtful clinical presentation of stroke which required MRI confirmation prior to receiving tPA.

Baseline-characteristics according to allocation are presented in table 2 and according to actual image-modality conducted in table 3+4.

Of the total number of patients presenting with symptoms of acute stroke, 140 (29.7%) were treated with iv-tPA of which 8 (5.7%) were later discharged with a stroke-mimic diagnosis.

Duration of CT and MRI-based evaluation:

For iv-tPA-treated patients, the median DNT for CT-allocated patients was eight minutes shorter than for MRI-allocated patients ($p=0.004$) (table 5). For patients with ischemic stroke, both CT-based DDT and DNT were significantly shorter; both according to allocation ($p<0.005$) and according to actual image-modality performed ($p<0.002$) (table 6+7).

For patients with discharge-diagnosis of ICH, TIA or stroke-mimics, DDT was not significantly different for CT-based and MRI-based evaluation (table 5-7).

The time from admission to image-initiation (Door-Scan-Time (DST)) was significantly shorter on CT-days for both Ischemic stroke and TIA-patients, both according to allocation and imaging conducted without cross-overs (table 5+6).

No systematic time-dependent change in DNT were observed during the trial-period for CT ($p=0.277$) nor MRI ($p=0.777$)-based assessment.

Predictors of DDT and DNT:

Only MRI-allocation predicted DDT (table 8) and DNT (table 9) when allowed for the cluster-effect of the stroke-physicians and adjustment for; age, gender, stroke-severity, cross-over, stroke-physician-seniority, the business of the shift and for DDT in addition for pre-onset-mRS, discharge-diagnosis and additional image-sequences added to the SOP.

Compared to MRI-allocated patients, the multilevel-models predicted a 24.0% shorter DDT ($p=0.0001$) and a 27% shorter DNT ($p=0.008$) for CT-allocated patients, table 8+9.

Modified Rankin Scale at three month for iv-tPA-treated patients:

Pre-mRS did not differ for CT (median 1.0 IQR 3.0) versus MRI-allocated (median 0.0 IQR 2.0) iv-tPA-treated patients ($p=0.096$).

When adjusted for pre-mRS, mRS at three month did not differ between CT ($n=72$, median 2.0 IQR 2.0) and MRI ($n=60$, median 1.0 IQR 4.0) allocated iv-tPA-treated patients, $p=0.275$.

Predicted long-term outcome for MRI-examined patients due to treatment-delay:

When the paired predicted four outcomes were compared for each patient, only the chance of independent living differed between the two scenarios: Admission of a CT versus and MRI-day. The COMPASS-tool did not for any of the iv-tPA-treated MRI-allocated patients predict a change in the risk of SICH or death within three months as a consequence of the median 8 minutes longer MRI-allocated assessment.

For eleven (16.9%) of the 65 iv-tPA-treated MRI-allocated patients the predicted chance of independent living ($mRS<3$) at 3 months increased with 1% when the patient's individual prediction were repeated with an 8 minutes shorter ONT; equaling the patients' true individual

ONT subtracted the 8 minutes difference between the median DNT for CT and MRI-allocated patients (table 5). The difference in predicted chance of independent living if admitted on a CT versus an MRI-day did not exceed one percent for any of the 65 iv-tPA-treated MRI-allocated patients.

Discussion:

DNT were 8 minutes shorter for CT-allocated patients compared to MRI-allocated patients; a time-difference that by simulated prediction decreased the chance of independent living at 3 months with 1% in 16.9% of the MRI-allocated iv-tPA-treated patients.

MRI was not feasible in 23.7% of the MRI-allocated patients due to MRI-contraindications and in additional 14.2% due to clinically conditions not compatible with safely conduction of MRI of diagnostic quality. In 9.8% of the CT-allocated patients MRI was conducted to avoid X-ray irradiation in pregnant or young patients or to establish the correct diagnosis prior to potential iv-tPA administration.

So far no previous randomized trial has compared DNT for CT versus MRI-allocated stroke-patients. This quasi-randomized trial comparing CT versus MRI as first-line of brain-imaging in acute stroke patients was conducted in a stroke-unit conducting approximately 300 iv-tPA-treatments each year. The iv-tPA-function is based on a well-organized set-up with guidelines for both evaluation and acute stroke-treatment.

The study shows that MRI is a potential option in the acute stroke-setting— though significantly slower and less often feasible than CT. The study does not allow for assessment of the potential additional and clinically useful image-information gained when patients have MRI.

The quasi-randomization allocated the patients into two well-balanced groups though males were more prevalent in the MRI-allocated group.

The per-protocol-groups differed in both numbers and baseline-characteristics due to diverse clinical presentations, inherent MRI-contraindications and in some cases need of additional imaging.

We wished to compare the use of CT and MRI in a clinical setting with patients reflecting patients with symptoms of acute stroke being brought to an acute stroke-unit for iv-tPA-assessment. Consequently no inclusion and exclusion-criteria were applied apart from a lower age limit and iv-tPA-treatment-initiation within 4.5 hours from onset. Consequently the cohort includes patients with discharge-diagnosis of stroke, TIA as well as stroke-mimicking conditions.

We did not observe a change in DNT for either CT or MRI-allocated patients throughout the trial-period, indicating that a potential gained accumulative experience of the stroke-team did not influence the effectiveness of the patient-assessment.

Our MRI-protocol to rule out ICH prior to iv-tPA takes a total of 6.4 minutes compared to 17.3 seconds for the non-contrast CT head. Shorter MRI-based protocols have been introduced (5) and could if used potentially have reduced the 8-minutes time-difference between CT and MRI-based evaluation. As previously reported (6), the interpretation of MRI-sequences can be initiated while the MRI is still underway contrary to how the CT-head must be completed before the image-interpretation can be begun; consequently at least part of the treatment-delay caused by the longer MRI-protocol is reduced.

Further MRI-safety is imperative and prolongs DNT in ways not inflicting CT-based evaluation; no time is devoted on ruling out MRI-contraindications or physical agitation affecting the diagnostic image-quality is less pronounced. Even instructions and positioning of the patient in the MRI-scanner are usually more time-consuming compared to CT.

In Helsinki (1), patients were transferred directly from the ambulance-stretcher to the CT-bed which is not feasible in a MRI-based acute setting as contraindications needs to be ruled out before the patient enters the MRI-room. To unify and thus be able to compare the CT and MRI-based setup, all patients were received in the dedicated stroke-room on CT as well as MRI-days.

Due to a limited number of patients, we were not allowed to test further predictors of DDT and DNT in our random-effect-models.

We did not identify seniority of the stroke-physician as well as the work-intensity during the shift as predictors of DDT or DNT.

As previously reported, nor gender or age of the patient (7, 8) or stroke-severity on admission (7) predicted DNT.

As no patients were missed and DDT and DNT were registered for all patients, patient-bias does not influence the DNT-related results but for a total of 8 iv-tPA-treated patients it was not possible to obtain the three-month-follow-up mRS by telephone.

Neither allocation-concealment nor blinding of patients and stroke-team-members were possible due to the clinical quasi-randomized setup and the nature of the CT and MRI-equipment.

The allocation demonstrates a scenario of a hospital being either CT or MRI-based with MRI-contraindications and clinical indications enforcing cross-overs from the primary chosen image-modality. Deviations from the allocated imaging, on both CT and MRI-days potentially prolong DNT, though cross-overs were not identified as predictors of DDT or DNT in our random-effect-model.

Hundred-seven (48.9%) of the MRI-allocated patients and 22 (9.7%) of the CT-allocated patients had a cross-over to the non-allocated image-modality. Detection of a pacemaker, ferromagnetic implants or a body size too large to fit in the MRI-scanner are objective exclusion criteria, whereas

assessment of critically ill patients' suitability for MRI is based on empirical experience and a situational evaluation of the individual patient. Unlike previous studies (17, 20, (9), we did not use immobilization of the patients' heads or upper extremities or medical sedation to increase the number of MRI eligible patients otherwise too agitated for MRI of diagnostic quality. Nor did we use MRI-compatible monitoring of vital values or excluded patients with substantial functional deficits to increase the frequency of MRI-eligible patients (17, 20). Previous studies on selected acute stroke patients have reported MRI-contraindications in 3.1-12.4% of the examined patients (15, 17-19). Singer et al (10) further excluded acute stroke patients with reduced pre stroke functional status (mRS>1) who are more likely to have comorbidities resulting contraindications to MRI. Consequently our population included a higher number of patients with MRI-contraindications (23.7%) compared to the previous reported studies.

This single-center trial includes patients with mixed socioeconomic-status being admitted to an acute stroke-unit in a public Danish hospital; no private hospitals accept acute stroke-patients. We believe that our results generalizes what needs to be done in the acute setting; the patient-history and blood-samples should be obtained, the physical examination performed and imaging conducted and interpreted to rule out ICH prior to iv-tPA-administration (1). The trial was conducted on weekdays during daytime and does thus not generalize to off-hours and weekends.

Though the COMPASS-simulation-tool predicted that chance of independent living at 3 months decreased with 1% in 16.9% of the iv-tPA-treated MRI-allocated patients due to the median treatment-delay of 8 minutes compared to CT-allocated patients, it is important to stress that the inferior outcome in MRI-examined patients is based on predictions and not true established long-term outcomes. Further did the mRS at three months indeed not differ between our iv-tPA-treated CT versus MRI-allocated patients. The comparison was though based on a limited number of CT versus MRI-allocated patients and is likely not sufficiently powered. Long-term outcome has further previously been reported to be influenced by various patient-dependent factors (11-17). It is likely that a trial with a greater number of patients would be able to detect a difference in outcome between CT and MRI-allocated patients.

To justify a potential time-related reduction in long-term outcome MRI must contribute with a higher diagnostic quality; in terms of a higher level of treatment-certainty or better still a lower frequency of iv-tPA-induced complications due to a more qualified selection of iv-tPA-candidates. As a large number of the patients were not able to have an acute MRI, use of MRI as first-line of brain-imaging is not uncomplicated. It is essential to have access to acute CT in case of patients with contraindications or patients unfit for MRI. Finally if MRI-based, one must consider the potentially treatment-delay in patients in need of CT instead of MRI.

Collaborating previous studies (1, 18), we had a low frequencies of iv-tPA treated patients with stroke-mimicking discharge-diagnosis in both the CT and the MRI-allocated groups; proving that fast and efficient assessment is attainable without compromising a high number of non-eligible patients.

Conclusion:

CT-based evaluation is significantly faster and more feasible than MRI-based assessment. In simulated prediction, the MRI-induced treatment-delay of 8 minutes potentially translates into a 1% decreased chance of independent living (mRS<3) at 3 months in 16.9% of the iv-tPA-treated MRI-allocated patients— though not supported by the clinically reported mRS at three months.

Conflicting interests:

The Authors declare that there is no conflict of interest

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Tables and figures:

Fig 1. Flow chart of patients.

Door-needle-time (DNT), Intravenous-tissue-Plasminogen-Activator (iv-tPA), modified-Rankin-Scale (mRS), Computer Tomography (CT) and Magnetic Resonance Imaging (MRI).

MRI-allocation (n=219)	Received MRI (n=112)		
	Cross-over to CT (n=107)	Contraindications (n=52)	Pacemaker (n=15)
			Ferromagnetic implants (n=5)
			Orbital metal splinters (n=1)
			Too large body size (n=8)
			Claustrophobia (n=6)
			Cervical hyperkyphosis (n=2)
			Explicit suspicion of MRI-contraindications (n=15)
		Clinical condition (n=40)	Critical medical condition (n=14)
			Physical unrest (n=17)
			Need for CT-angiography including cervical vessel (n=9)
		Organization (n=15)	Waiting time for MRI > 10 minutes (n=13)
			Close to iv-tPA-window (n=1)
			Simultaneous arrival of >1 patient (n=1)
CT-allocation (N=225)	Received CT (n=203)		
	Cross-over to MRI (n=22)	X-ray-related (n=6)	Age < 30 years of age (n=5)
			Pregnancy (n=1)
		Needed for diagnostic clarification (n=16)	Clinical suspicion of space-occupying tumor (n=4)
			Diagnostic need for radiological signs of acute ischemia in patients with atypical clinical presentation (n=11)
			Suspicion of medullar compression (n=1)

Table 1 Cross-overs from allocated image modality

	CT-allocated n= 225	MRI-allocated n= 219	p
Age, years*	70 (26)	70 (24)	0.757
Male gender	97 (44.1%)	118 (53.9%)	0.030
NIHSS admission*	3 (7)	3 (6)	0.838
mRS before onset*	1 (2)	1 (2)	0.743
Thrombolysis	75 (33.3%)	65 (29.7%)	0.468
Endovascular treatment	7 (3.1%)	6 (2.7%)	0.817
Hypertension	91 (40.4%)	86 (39.3%)	0.876
Hypercholesterolemia	56 (24.9%)	47 (22.4%)	0.457
Atrial fibrillation	35 (15.6%)	40 (18.3%)	0.552
Diabetes melitus	19 (8.4%)	26 (11.9%)	0.299
Previous stroke/TIA	52 (23.1%)	54 (24.7%)	0.787
Alcohol abuse	23 (10.2%)	21 (9.6%)	0.974
Use of tobacco	47 (20.9%)	42 (19.2%)	0.777
Discharge diagnosis			
Ischemic stroke	96 (43.6%)	89 (40.6%)	0.736
TIA	40 (17.8%)	42 (19.2%)	0.797
ICH	15 (6.7%)	22 (10.0%)	0.264
Stroke-mimic	74 (32.9%)	66 (30.1%)	0.502

Table 2, Baseline characteristics for CT and MRI-allocated patients, *median (IQR)

	CT performed n= 310	MRI performed n= 134	p
Age*	73.5 (22)	63.5 (29.25)	0.001
Male gender	148 (47.7%)	67 (50%)	0.739
NIHSS admission*	4 (10)	2 (5)	0.001
mRS before onset*	1 (3)	0 (1)	0.001
Thrombolysis	107 (34.5%)	33 (24.6%)	0.051
Endovascular treatment	12 (3.9%)	1 (0.7)	0.059
Hypertension	134 (43.2%)	43 (32.1%)	0.036
Hypercholesterolemia	76 (24.5%)	27 (20.1%)	0.380
Atrial fibrillation	56 (18.1%)	19 (14.2%)	0.387
Diabetes melitus	36 (11.6%)	9 (6.7%)	0.162
Previous stroke/TIA	77 (24.9%)	29 (21.6%)	0.546
Alcohol abuse	32 (10.3%)	12 (9.0%)	0.798
Use of tobacco	62 (20.0%)	77 (57.5%)	0.980
Discharge diagnosis			
Ischemic stroke	140 (45.2%)	45 (33.6%)	0.030
TIA	54 (17.4%)	28 (20.9%)	0.463
ICH	29 (9.4%)	8 (6.0%)	0.319
Stroke-mimic	87 (28.1%)	53 (39.6%)	0.023

Table 3, Baseline Characteristics for CT and MRI-examined patients according to imaging performed (cross-overed patients included), *median (IQR)

	CT-allocated n= 203	MRI-allocated n= 112	p
Age*	71 (23)	67 (26.25)	0.001
Male gender	92 (45.3%)	62 (55.4%)	0.112
NIHSS admission*	3 (8)	2 (4)	0.006
mRS before onset*	1 (2)	0 (1)	0.001
Thrombolysis	73 (36.0%)	31 (27.7%)	0.170
Hypertension	88 (18.8%)	40 (35.4%)	0.230
Hypercholesterolemia	55 (27.1%)	26 (23.2%)	0.536
Atrial fibrillation	33 (16.3%)	17 (15.0%)	0.929
Diabetes melitus	19 (9.4%)	9 (8.0%)	0.851
Previous stroke/TIA	48 (23.6%)	25 (22.3%)	0.899
Alcohol abuse	23 (11.3%)	12 (10.7%)	0.889
Use of tobacco	41 (36.6%)	21 (21.4%)	0.885
Discharge diagnosis			
Ischemic stroke	94 (46.3%)	43 (38.4%)	0.316
TIA	34 (16.7%)	22 (19.6%)	0.625
ICH	15 (7.4%)	8 (7.1%)	0.936
Stroke-mimic	60 (29.6%)	39 (34.8%)	0.403

Table 4, Baseline Characteristics for CT and MRI-examined patients according to allocation (cross-overed patients excluded), *median (IQR)

			Onset-door-time		Door-scan-time		Door-decision-time		Door-needle-time		
		n	Minutes*	p	Minutes*	p	Minutes*	p	n	Minutes*	p
All patients	CT	225	89 (76)	0.870	9 (7)	0.001	19 (13)	0.001			
	MRI	219	87.0 (75.0)		12 (9.0)		23 (15.0)				
Ischemic stroke	CT	96	84.5 (68)	0.629	8 (7.5)	0.003	17 (11)	0.009	72	22 (16)	0.005
	MRI	89	80.5 (77.8)		10 (10)		23 (13.0)		60	30 (14)	
ICH	CT	15	81 (45)	0.891	8 (6.5)	0.169	16 (9)	0.371			
	MRI	22	75 (53)		13.5 (11.75)		18.5 (12)				
TIA	CT	40	102 (86)	0.937	9 (5.25)	0.002	20 (14.5)	0.089			
	MRI	42	97 (91.5)		13.5 (9)		25 (17)				
Stroke-mimics	CT	74	92.5 (93.25)	0.859	11 (12.5)	0.329	19 (10.75)	0.169	3	25	0.571
	MRI	66	107.5 (89.5)		11 (9.25)		23.5 (17.5)		5	41 (36)	
All iv-tpA-treated patients	CT	75	84.5 (72)	0.136	8 (6)	0.001	16.5 (10)	0.001	75	22 (15.5)	0.004
	MRI	65	71 (74)		9.75 (9.75)		23 (12.0)		65	30.0 (14.0)	

Table 5, Time intervals for patients according allocation and discharge diagnosis. *Minutes, median (IQR)

		n	Onset-door-time		Door-scan-time		Door-decision-time		Door-needle-time		
			Minute s*	p	Minutes*	p	Minutes*	p	n	Minutes*	p
All patients	CT	203	89.0 (77.5)	0.940	8.5 (8)	0.001	18 (12.5)	0.001			
	MRI	112	92 (81.5)		12.5 (11)		26 (15)				
Ischemic stroke	CT	94	88 (71.5)	0.620	8 (7.5)	0.038	17 (11)	0.001	70	22 (15.5)	0.001
	MRI	43	94 (82)		10 (10.5)		26 (13.5)		30	32 (12.5)	
ICH	CT	15	81 (45)	0.428	8 (6.5)	0.053	16 (14)	0.089			
	MRI	8	70.5 (44.3)		16 (6.8)		25.5 (13.8)				
TIA	CT	43	90 (85.5)	0.918	8.5 (4.8)	0.002	20 (14)	0.077			
	MRI	22	89 (84.3)		14.5 (9.5)		25 (17)				
Stroke-mimics	CT	60	100 (83.8)	0.823	10 (12)	0.226	19 (12)	0.139	3	25	0.500
	MRI	39	100.2 (95.5)		12 (9.8)		27 (20)		1	51	
tpA-treated patients	CT	73	88 (72.8)	0.420	8 (6)	0.006	16 (10)	0.001	73	22 (15)	0.001
	MRI	31	84.5 (84.3)		11 (9)		25 (13.5)		31	34 (14)	

Table 6; Time intervals for patients according to allocation, cross-overed patients excluded. * Minutes, median (IQR)

		N	Onset-door-time		Door-scan-time		Door-decision-time		Door-needle-time		
			Minutes*	p	Minutes*	p	Minutes*	p	n	Minutes*	p
All patients	CT	310	88.0 (71.0)	0.929	10 (7.5)	0.001	19 (12)	0.001			
	MRI	134	89.5 (79.8)		12 (10.3)		25 (15)				
Ischemic stroke	CT	140	80.0 (67.0)	0.557	9 (7.5)	0.175	18 (11.25)	0.001	100	23 (17.0)	0.002
	MRI	45	82 (85)		10 (9.8)		26 (13.8)		32	32 (14)	
ICH	CT	29	82.5 (56.5)	0.307	10 (8)	0.061	16 (8)	0.05			
	MRI	8	70.5 (44.3)		16 (6.8)		25.5 (13.8)				
TIA	CT	54	100 (88.5)	0.982	10 (6.8)	0.009	21 (14)	0.170			
	MRI	28	102 (88.5)		13 (9)		25.5 (17.3)				
Stroke-mimics	CT	87	103.5 (80.5)	0.476	11 (10)	0.177	20 (12)	0.196	7	25 (27)	0.250
	MRI	53	84.5 (93.3)		12 (10)		22.5 (17)		1	51	
tpA-treated patients	CT	107	80 (67.5)	0.511	9 (7)	0.036	17 (12)	0.001	107	23.0 (16.5)	0.001
	MRI	33	78 (84.5)		11 (9)		26 (13.8)		33	34 (14)	

Table 7, Time intervals for patients according to imaging conducted, cross-overs included. *Minutes, median (IQR)

	Estimate	Standard Error	95% CI	Significance
Intercept	21.677	1.166	16.018-29.336	0.0001
Age	0.999	1.001	0.997-1.002	0.763
Female gender	1.087	1.054	0.980-1.208	0.115
NIHSS on admission	0.998	1.005	0.989-1.008	0.749
mRS prior onset	1.009	1.022	0.967-1.052	0.685
CT allocation*	0.760	1.068	0.668-0.864	0.0001
Cross-over to CT for MRI-allocated patients	1.097	1.067	0.964-1.246	0.153
Cross-over to MRI for CT-allocated patients	0.952	1.139	0.737-1.29	0.703
Neurological consultant**	1.117	1.091	0.914-1.366	0.241
Senior stroke neurological consultant**	1.165	1.091	0.913-1.268	0.093
Ischemic stroke***	1.076	1.087	0.913-1.144	0.378
Transitory Ischemic Attack***	1.150	1.082	0.985-1.343	0.077
Intracranial Hemorrhage***	0.913	1.122	0.729-1.144	0.429
No tPA-prescribed	1.080	1.085	0.920-1.269	0.346
Minutes to arrival of next patient, intervals of 20 minutes	0.987	1.007	0.973-1.001	0.077
Number of patients evaluated during shift	0.993	1.024	0.948-1.041	0.7769
Additional imaging performed	1.097	1.075	0.952-1.264	0.200

Table 8 Random effect multilevel model identifying predictors of “door-decision-times” and allowing the cluster effect of the 24 stroke physicians. The dependent variable door-to-decision-time was log10-transformed to comply with test assumptions; estimates, Standard Errors and CI have been backtransformed.

* Versus MRI-allocation, **versus Late neurological resident, *** versus stroke mimic discharge diagnosis

	Estimate	Standard Error	95% CI	Significance
Intercept	37.350	1.350	20.587-67.764	0.0001
Age	1.002	1.003	0.995-1.008	0.627
Female gender	1.189	1.096	0.991-1.426	0.063
NIHSS on admission	0.985	1.008	0.971-1.000	0.054
CT-allocation*	0.730	1.123	0.5580-0.920	0.008
Cross-over to CT for MRI-allocated patients	1.457	1.127	0.912-1.468	0.226
Cross-over to MRI for CT-allocated patient	1.111	1.416	0.557-2.215	0.763
Neurological consultant* *	0.986	1.183	0.699-1.391	0.935
Senior stroke neurological consultant **	1.077	1.221	0.971-1.605	0.054
Minutes to arrival of next patient, intervals of 10 minutes	0.980	1.013	0.956-1.005	0.123
Number of patients evaluated during shift	0.945	1.047	0.863-1.035	0.219

Table 9 Random effect multilevel model identifying predictors of “door-needle-times” and allowing the cluster effect of the 24 stroke physicians. The dependent variable door-to-decision-time was log10-transformed to comply with test assumptions; estimates, Standard Errors and CI have been back-transformed.

*versus MRI-allocation performed, **versus Late neurological resident