NHS Greater Glasgow and Clyde

CLINICAL GUIDELINE

Iodine based contrast media and gadolinium based contrast agents in adults

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

The administration of iodine based contrast media and gadolinium based contrast agents in adults

NHS GG&C Guidelines

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Contents

NHS GG&C Contrast Guidelines for Adults

This guidance exists to inform the safe use of contrast media in NHS GGC in patients aged 16 or over.

Iodine Based Contrast Media

The guidance has been updated in line with the Royal College of Radiologist's adoption of the Royal Australian and New Zealand College of Radiologists published in 2018 [1].

Guidance has been split into sections for intravenous and intra-arterial procedures.

The NICE guidance on acute kidney injury published in December 2019 has been reviewed, but where the guidelines conflict the principles of the RANZCR guidance has been adopted as more up to date in relation to use of contrast media.

Gadolinium Based Contrast Agents

This guidance is based on the Royal College of Radiologists guidance published 2019 [2].

CT – Intravenous Iodine Based Contrast Media

Contrast and renal impairment:

- In emergency imaging (trauma, acute bleeding, stroke etc.) the scan should not be delayed for lack of a recent eGFR.
- Contrast should be given regardless of the patient's renal function if the benefit to the patient outweighs the risks - this will be justified by the radiologist in discussion with the clinical team.
- Risk of post-contrast acute kidney injury (PC-AKI) in patients with a stable eGFR >30 ml/min is likely to be very low or non-existent, therefore this does not require additional clarification from a radiologist.
    - Universal recommendation of peri-hydration is not recommended in this group. Patients, however, who have acutely deteriorating renal function may benefit from peri-hydration measures.
- Severely reduced renal function (eGFR <30ml/min) is not a contraindication to i.v. contrast if it is clearly clinically indicated. Careful consideration however is required by the radiologist and the clinical team.
    - These patients may benefit from peri-hydration and contrast dose minimisation.

Requirement for up-to-date eGFR

Severe renal function impairment is rare in patients who are not aware that they have diabetes and/or kidney disease.

Inpatients who are acutely unwell may have an unexpected acute kidney injury, and so a recent eGFR should be sought. If not mentioned on the request, it is likely they will have had an eGFR during the admission, Trak or Portal should be checked.

Outpatients without an up-to-date eGFR should be asked the following:

- Do they have kidney disease or a kidney transplant?
- Are they diabetic?
- Are they taking Metformin?

If any of the above risks are present, then a recent eGFR is required. No recommendation is given for a time period regarded as "recent" in the RANZCR guidelines. They suggest this should instead be governed by clinical judgement based on the likelihood that renal function has deteriorated to a significant degree since last tested.

Locally an eGFR within 3 months is accepted, as detailed in the RCR guidelines.

Low eGFR

- If eGFR <30ml/min, discuss with a radiologist before administering contrast.
- Base contrast dose upon the minimum required for the type of scan and patient's weight.
- Recommend peri-hydration as per guidance below.

Peri-hydration in those with renal impairment

- For inpatients, the renal service recommends i.v. hydration with 0.9% Saline to prevent post-contrast acute kidney injury, as follows.

> **Inpatient Post Contrast Instructions**
>
> The renal service recommends iv hydration in inpatients to prevent post-contrast acute kidney injury, as follows:
>
> Give iv saline if:
> - eGFR<30ml/min
>
> Suggested regime
> - 0.9% i.v. saline, 250ml over 1 hour BEFORE contrast &
> - 0.9% i.v. saline, 500ml over 4-6 hours AFTER contrast
>
> Avoid i.v. fluid if extracellular fluid overload or heart failure

- The need for peri-hydration should be identified at the vetting stage and communicated to the ward.
- The advice could be included on a sticky label or A5 sheet and sent back to the ward with patients following their scan as a reminder.
- Printed labels are available for this purpose, DR-GGC-FORM-030.

- For outpatients with eGFR <30ml/min the renal service does not make any specific recommendation.
- If there is a good indication for i.v. contrast, do not withhold it.
- Do not restrict clear fluids prior to a scan.
- Encourage outpatients to drink plenty of water before, and again after, the scan.
- Ask outpatients to see their GP or clinician to get their renal function checked at 10-14 days post contrast, unless a blood test already done 3-9 days after the procedure indicated they had not developed AKI.
- A letter is available for this purpose, DR-GGC-FORM-029.

Metformin

For patients on Metformin there is a small theoretical risk of developing lactic acidosis if their renal fuction deteriorates further post contrast:

- Contrast can be administered as required.
- eGFR ≥ 30 ml/min:
  - Continue Metformin as normal following scan. No action required.
- eGFR <30 ml/min or unknown, or acutely unwell patient, or patient who has acutely declining renal function:
  - Stop Metformin from the time of contrast administration.

- Ask the responsible clinician to arrange monitoring of renal function and advise the patient when Metformin should be restarted, or to seek guidance from the patient's diabetic specialist.

- A letter is available for this purpose, DR-GGC-FORM-028.

Other considerations

Allergies & Asthma

- The patient should be asked about previous reactions to contrast media, and these should be documented in detail in CRIS alarms (contrast type, dose, severity of reaction and treatment).
- The patient should be asked about other severe or life-threatening allergies (anaphylaxis) and severe or unstable asthma.
- If the patient answers positively to either of the above, seek advice from a radiologist before injecting contrast.
- If the patient suffers a reaction after administering contrast, document this in CRIS alarms, and in the Event Comments, including the exact contrast used, nature of reaction, severity of reaction, treatment given and date. Involve a radiologist. The patient and referring clinician should be advised that the patient should be referred to the Drug Allergy service for testing in order to determine which contrast media may be safely used in future.

Breast feeding

- Intravenous iodine based contrast administration is safe. There is no need to cease breastfeeding or discard milk after i.v. contrast, though if patients ask, they are welcome to do so.

Haemodialysis

- It is safe to administer contrast to patients on established haemodialysis.
- There is no need to expedite dialysis after contrast administration.

Phaeochromocytoma

- Intravenous contrast administration is safe for patients known or suspected of having a phaeochromocytoma. No specific precautions are required.

Thyrotoxicosis:

- Iodine based contrast should not be administered intravenously to patients who have untreated hyperthyroidism. Treatment (usually β-blockers and carbimazole) should be initiated by the referring clinician first.
- In the emergency situation contrast may be administered and endocrinological advice sought afterwards, as thyrotoxicosis can take weeks to occur after contrast administration.
- Patients with a hyperfunctioning nodule, with or without multinodular goitre, are at increased risk of hyperthyroidism after contrast and should be warned, and monitored, in the following weeks.

Thyroid cancer

- Administration of iodine based contrast will prevent the use of radioactive iodine to treat thyroid cancer for up to 8 weeks afterwards.
- Give i.v. contrast, unless the referrer specifies in the clinical history to avoid iodine. Check the clinical history carefully (guidance agreed with GGC oncologists).

Myasthenia Gravis

- Symptoms including breathing difficulties may be worsened after i.v. iodine based contrast contrast, although this is rare (approx 5%). Acute deterioration with myasthenic crisis has been reported and thus these patients should be observed for longer in the department and only be scanned at sites with resuscitation teams available. Patients should be made aware of the small risk and told to report any worsening of symptoms.

Sickle Cell Disease

- No known serious medical risk but patients may experience temporary worsening of pain and should be informed of this.

Pregnancy

- Due to theoretical risk to the foetal thyroid gland, TFTs should be checked after birth.
- As this is routine in the UK (heel prick test), no special precautions are necessary.

CT Checklist

- The guidance has been incorporated into an updated CT Checklist to be available in all NHSGGC CT rooms, and used by CT radiographers for all patients, DR-GGC-PROC-045.
- Note the checklist includes some other elements unrelated to contrast medium use.
- The Checklist is available on Q-Pulse, and is reproduced in the appendix.

Summary

In the **inpatient** population:

- An up-to-date eGFR (this admission) is required to exclude unexpected acute kidney injury.
- Patients who have acutely deteriorating kidney function, regardless of eGFR value, are at risk of developing a PC-AKI.
- Risk of giving i.v. iodine based contrast in patients with eGFR >30 ml/min is very low / non-existent therefore clarification by a radiologist is not required.
- An eGFR <30 ml/min is not an absolute contraindication to i.v. contrast but this should be a radiologist/clinician decision. If contrast is indicated, it should normally be given.
    - These patients may benefit from intravenous peri-hydration.
    - Contrast dose should be tailored based upon scan type and patient weight.

In the **outpatient** population:

- An up-to-date eGFR (preferably within 3 months) is required if the patient answers yes to any of the following:
    - Kidney disease or kidney transplant
    - Diabetes
    - On Metformin
- Age and heart failure no longer need to be considered as specific risk factors.
- If eGFR <30 ml/min, give contrast if it is indicated, but encourage good oral hydration and arrange for a check of renal function at 10-14 days.
- If the patient takes Metformin and eGFR <30 ml/min, Metformin should be stopped and the referrer should arrange to review renal function and advise the patient on restarting Metformin. This is due to the small risk of developing lactic acidosis.

Intra-arterial Iodine Based Contrast Media

Adhere to guidance for intravenous iodine based contrast.

Additional notes:

It is thought the risk from intra-arterial iodine based contrast is only higher than intravenous use when there is first pass contrast entering the renal arteries (e.g. thoracic angiography, EVAR, renal angio & intervention).

For patients with eGFR<30 ml/min

- For outpatients, encourage oral hydration, as per intravenous contrast use.
- Outpatients may need Day Case admission for i.v. perihydration.
- For inpatients, and those subjected to first pass renal contrast, follow the guidance for i.v. peri-hydration.

Metformin

For patients on Metformin who are exposed to first pass renal contrast, or risk of renal embolisation:

- eGFR ≥ 45 ml/min:
    - Continue Metformin as normal.
- eGFR <45 ml/min or unknown, or high contrast volumes, or risk of renal procedural injury:
    - Stop Metformin from the time of contrast administration.
    - Ask the responsible clinician to arrange monitoring of renal function and advise the patient when Metformin should be restarted, or to seek guidance from the patient's diabetic specialist.

MRI – Gadolinium Based Contrast Agents (GBCAs)

Allergies & Asthma

- The patient should be asked about previous reactions to contrast agents, and these should be documented in detail in CRIS alarms (contrast type, dose, severity of reaction and treatment).
- The patient should be asked about other severe or life-threatening allergies (anaphylaxis) and severe or unstable asthma.
- If the patient answers positively to either of the above, seek advice from a radiologist before injecting contrast.
- If the patient suffers a reaction after administering contrast, document this in CRIS alarms, and in the Event Comments, including the exact contrast used, nature of reaction, severity of reaction, treatment given and date. Involve a radiologist. The patient and referring clinician should be advised that the patient be referred to the Drug Allergy service for testing in order to determine which contrast media may be safely used in future.

Gadolinium Retention

Health concerns have been raised about retention of tiny amounts of gadolinium in the body including in the brain, the consequences if any of which are currently under investigation – the research to date is very reassuring. Following a precautionary principle there were changes to the marketing authorisations for GBCAs in 2018 and withdrawal of older 'less stable' compounds for intravenous use. The current status is as below [3]:

- The cyclic chelate GBCAs, Dotarem, Clariscan, ProHance and Gadobutrol, remain available for i.v. use, using the lowest dose effective for diagnosis.
- The linear chelate GBCAs, MultiHance and Primovist, remain available for liver imaging studies only.
- The dilute linear chelate GBCA Magnevist for intra-articular use must only be used for MR arthrography.

For all contrast-enhanced MRI scans the agent used and dose must be recorded in the Process screen for the examination in CRIS.

Renal Impairment

Although gadolinium contrast agents are potentially nephrotoxic in large volumes this is not an issue with the small doses used for enhancing MRI scans and no special precautions are required in this respect.

Nephrogenic Systemic Fibrosis (NSF) is a very rare condition previously identified in patients with severe renal failure on dialysis, and associated with the use of those linear Gadolinium contrast agents that have been subsequently withdrawn from EU and UK use.

Although NSF does not appear to be a risk with the GBCAs we now use the precautionary principle remains in place for patients with renal failure.

- Ask, does the patient have kidney disease, a renal transplant, or diabetes, or are they an inpatient? If so, check eGFR.
- For patients undergoing lower limb MR angiography, if eGFR <30 ml/min, use the non-contrast QISS technique as the initial investigation. Contrast-enhanced MRA may be used subsequently if this non-contrast MRA has not been sufficiently diagnostic.
- For all other contrast enhanced MRI scans, if eGFR <20 ml/min or with acute kidney injury, discuss with radiologist for consideration of non-contrast techniques or alternative imaging modalities initially. If contrast is clinically indicated, use the lowest dose possible and do not repeat within 7 days. Discuss with nephrologist whether any alterations to dialysis schedule are indicated prior to scan (see haemodialysis, below).
- For patients with eGFR 20-59 ml/min, GBCAs can be used with no specific restrictions, but do not repeat within 7 days.

Other considerations

Breast Feeding

- A very small percentage of an injected dose of GBCA enters the breast milk but virtually none is absorbed across the normal infant gut. No special precaution, discarding of milk or cessation of breastfeeding is required, though if patients ask, they are welcome to do so.

Pregnancy

- There is a lack of data on the use of GBCAs in pregnancy and hence they should not be used during pregnancy unless the clinical condition of the patient makes their use absolutely necessary. However, if they must be used then no effect on the developing foetus is anticipated based on the current limited evidence.

Haemodialysis & Peritoneal Dialysis

- Avoid gadolinium contrast administration without discussing with nephrologist – although extremely rare, NSF can occur months after gadolinium dosing and therefore it would be sensible to inform the clinical team who regularly follows up the patient.
- For patients already on regular dialysis, if gadolinium is necessary, discuss with the renal team in advance and schedule scan to permit haemodialysis as close as possible (and within 24 hours) of the contrast administration.

Miscellaneous

- GBCAs are safe for those patients taking Metformin, and those patients with thyroid disorders, sickle cell disease, phaeochromocytoma or myasthenia gravis.

MR Checklist

- The guidance has been incorporated into an MR Checklist to be available in all NHSGGC MR rooms, and used by MR radiographers for all patients, DR-GGC-PROC-057, in addition to the MR safety questionnaire.
- Note the checklist includes some other elements unrelated to contrast medium use.
- The Checklist is available on Q-Pulse, and is reproduced in the appendix.

Management of Reactions

Simple guidelines for the treatment of acute reactions, based on RCR Guidance [2].

Nausea/vomiting

- Transient: supportive treatment.
- Severe, protracted: appropriate anti-emetic drugs should be considered.

Urticaria

- Scattered, transient: supportive treatment, including observation.
- Scattered, protracted: appropriate H1-antihistamine orally or intramuscularly should be considered. Drowsiness and/or hypotension may occur.
- Profound: consider adrenaline 1:1000, 0.1-0.3 ml (0.1-0.3 mg) intramuscularly. Repeat, as needed.

Bronchospasm

- Oxygen by mask (6-10 l/min).
- β2-agonist metered dose inhaler (2-3 deep inhalations).
- Adrenaline:
    - Elevate patient's legs.
    - Normal blood pressure: adrenaline 1:1000, 0.1-0.3 ml (0.1-0.3 mg) intramuscularly.
    - Use smaller dose in a patient with coronary artery disease or elderly patient.
    - Decreased blood pressure: adrenaline 1:1000, 0.5 ml (0.5 mg) intramuscularly.

Laryngeal oedema

- Oxygen by mask (6-10 1/min).
- Adrenaline 1:1000, 0.5 ml (0.5 mg) intramuscularly. Repeat as needed.

Hypotension

- Isolated hypotension.
- Oxygen by mask (6-101/min).
- Intravenous fluid: rapidly, normal saline or lactated Ringer's solution.
- If unresponsive: adrenaline 1:1,000, 0.5 ml (0.5 mg) intramuscularly. Repeat as needed.

Vagal reaction (hypotension and bradycardia)

- Elevate patient's legs.
- Oxygen by mask (6-101/min).
- Atropine 0.6-1.0 mg intravenously, repeat if necessary. After 3-5 min, to 3 mg total (0.04 mg/kg).
- Intravenous fluids: rapidly, normal saline or lactated Ringer's solution.

Generalised anaphylactic reaction

- Call for resuscitation team.

- Suction airway if needed.
- Elevate patient's legs if hypotensive.
- Oxygen by mask (6-10 l/min).
- Adrenaline: 1:1000, 0.5 ml (0.5 mg) intramuscularly.
- H1 blocker, for example, chlorpheniramine 10-20 mg intravenously.

Recording and investigation of significant suspected contrast reactions

If the patient suffers a reaction after administering contrast, document this in CRIS alarms, and in the Event Comments, including the exact contrast used, nature of reaction, severity of reaction, treatment given and date. Involve a radiologist.

Discuss the patient's suspected contrast reaction with them and their carers, if appropriate, and provide written information.

The patient and referring clinician should be advised to consider referral to the West of Scotland Anaphylaxis Service for testing in order to determine which contrast media may be safely used in future.

Suspected adverse reactions should be reported on a Yellow Card to the MHRA.

Management of Extravasation

See the separate document *Guidance for the Prevention & Management of Contrast Medium Extravasation, DR-GGC-GUID-001*.

References

[1] RANZCR, “Iodinated Contrast Guidelines,” March 2018. [Online]. Available: https://www.ranzcr.com/college/document-library/ranzcr-iodinated-contrast-guidelines.

[2] RCR, “Guidance on gadolinium-based contrast agent administration to adult patients,” April 2019. [Online]. Available: https://www.rcr.ac.uk/system/files/publication/field_publication_files/bfcr193-gadolinium-based-contrast-agent-adult-patients.pdf.

[3] MHRA, “MHRA: Gadolinium-containing contrast agents: removal of Omniscan and iv Magnevist, restrictions to the use of other linear agents,” December 2017. [Online]. Available: https://www.gov.uk/drug-safety-update/gadolinium-containing-contrast-agents-removal-of-omniscan-and-iv-mag.

Appendix

The CT Checklist is reproduced here.

DR-GGC-PROC-045 CT Patient Check List (inc Radiographer Contrast Algorithm)	NHS Greater Glasgow and Clyde

This is an aide memoire only - not to be scanned in

PATIENT ID

- Patient ID checked? — Record on CRIS
- Examination explained to patient, and patient gives verbal consent — Record on CRIS

PREGNANCY

- Pregnancy check performed where appropriate? — Record on CRIS. Do not scan in.

CONTRAST ALLERGY, etc

- Previous contrast reaction? — If Yes, SEEK ADVICE
- Other serious allergies or severe or unstable asthma? — If Yes, SEEK ADVICE

POTENTIAL FOR RENAL ADVERSE REACTION

If eGFR Not Known

- Does the patient have kidney disease, a renal transplant, diabetes, or take metformin, or are they an inpatient?

If No, PROCEED anyway

If Yes, CHECK eGFR

If eGFR < 30, or no recent eGFR available — SEE OVER

If recent eGFR ≥ 30 — PROCEED

VETTING & PROTOCOL

- Examination has been vetted? And protocolled? — If unsure, CHECK CRIS
- Do you know which radiologist is supervising? — If unsure, SEEK ADVICE
- Is the exam code correct & appropriate? — If No, CHANGE IT on CRIS

CRIS DOCUMENTATION

- Dose and Contrast Batch information & Pregnancy Check, on Post Processing Screen
- Record any drugs given, scan issues or exceptional circumstances in Event Comments field
- Contrast Reaction, in Patient Alarms. Specify contrast used, what happened, and date.
- Contrast reaction, in Event Comments. Specify contrast used, what happened, treatment and advice given
- Note Patient checklist completed, in Event Comments field
- Check images are on PACS

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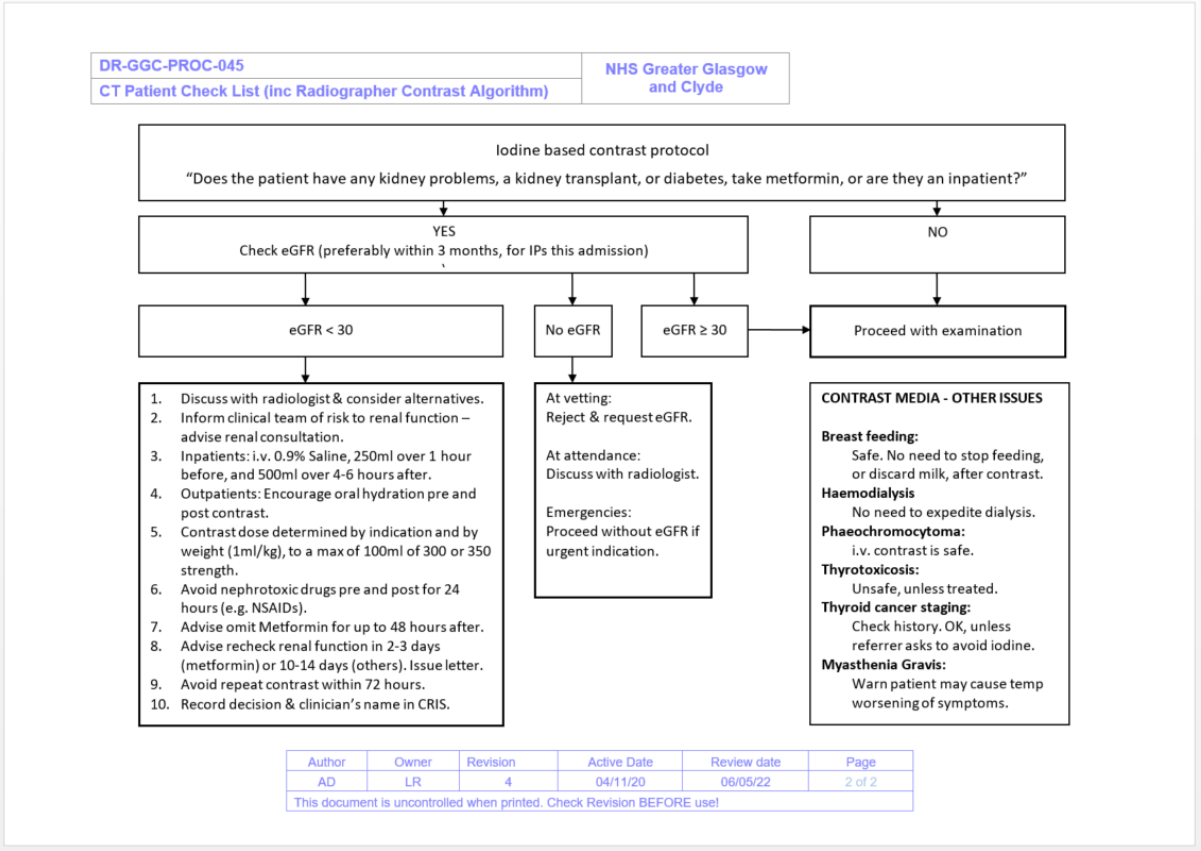

DR-GGC-PROC-045
CT Patient Check List (inc Radiographer Contrast Algorithm)
NHS Greater Glasgow and Clyde

Iodine based contrast protocol
"Does the patient have any kidney problems, a kidney transplant, or diabetes, take metformin, or are they an inpatient?"

YES
Check eGFR (preferably within 3 months, for IPs this admission)

NO

eGFR < 30

No eGFR

eGFR ≥ 30

Proceed with examination

1. Discuss with radiologist & consider alternatives.
2. Inform clinical team of risk to renal function – advise renal consultation.
3. Inpatients: i.v. 0.9% Saline, 250ml over 1 hour before, and 500ml over 4-6 hours after.
4. Outpatients: Encourage oral hydration pre and post contrast.
5. Contrast dose determined by indication and by weight (1ml/kg), to a max of 100ml of 300 or 350 strength.
6. Avoid nephrotoxic drugs pre and post for 24 hours (e.g. NSAIDs).
7. Advise omit Metformin for up to 48 hours after.
8. Advise recheck renal function in 2-3 days (metformin) or 10-14 days (others). Issue letter.
9. Avoid repeat contrast within 72 hours.
10. Record decision & clinician's name in CRIS.

At vetting:
Reject & request eGFR.

At attendance:
Discuss with radiologist.

Emergencies:
Proceed without eGFR if urgent indication.

CONTRAST MEDIA - OTHER ISSUES

Breast feeding:
Safe. No need to stop feeding, or discard milk, after contrast.
Haemodialysis
No need to expedite dialysis.
Phaeochromocytoma:
i.v. contrast is safe.
Thyrotoxicosis:
Unsafe, unless treated.
Thyroid cancer staging:
Check history. OK, unless referrer asks to avoid iodine.
Myasthenia Gravis:
Warn patient may cause temp worsening of symptoms.

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The CT Checklist is available on Q-Pulse, document DR-GGC-PROC-045.

The MR Checklist is also available on Q-Pulse, document DR-GGC-PROC-057.

Labels for peri-hydration for inpatients are available at DR-GGC-FORM-030.

Letters for patients requiring renal function checks post contrast are available on Q-Pulse

- DR-GGC-FORM-029 Renal Check Letter
- DR-GGC-FORM-028 Metformin Check Letter