Austin Health

Place Patient Label Here

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Austin Health, Heidelberg, Australia

Title	Using MRI to assess impact of add-on Empagliflozin on renal physiology in Type 2 diabetic patients
Short Title	Role of MRI in evaluating the impact of empagliflozin in patients with Type 2 diabetes
Project Sponsor	Royal Australian and New Zealand College of Radiologists. Radiology and Endocrinology Departments, Austin Health. Boehringer Ingelheim
Principal Investigator	Associate Professor Ruth Lim
Location	Austin Health

1 Introduction

You are invited to take part in this research project because you have Type 2 diabetes..

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

In diabetes, the kidneys absorb back a greater amount of glucose (sugar) than they should. Type 2 diabetes is diagnosed when glucose levels are higher than the normal range. This means the pancreas does not produce enough insulin and the insulin that is produced does not work as effectively. Long term high glucose levels can lead to complications such as kidney disease.

The main purpose of the study is to use a Magnetic Resonance Imaging (MRI) machine to assess how 2 medications used in the treatment of Type 2 diabetes affect the kidneys of patients with Type 2 diabetes.

Medications, drugs, and devices have to be approved for use by the Australian Federal Government. The medications we are using in this study are Empagliflozin and Sitagliptin, which are both approved in Australia by the Therapeutic Goods Administration (TGA) to treat Type 2 diabetes.

Empagliflozin is the medication we are most interested in studying using the MRI. It is a relatively new drug that helps the kidneys to remove excess glucose from the body and decrease the amount of glucose absorption. In addition to lowering blood glucose levels, it is thought it may also preserve long term kidney function of patients with existing kidney disease when added to their current diabetes medications.

Sitagliptin also lowers glucose levels however it works with the pancreas and the liver to get the body to release extra insulin, but only when blood glucose levels are high.

Empagliflozin will be compared to Sitagliptin, as Sitagliptin is not known to have an effect on kidney function.

MRI uses a powerful magnet to look at structures in the body, and can look at kidney structure as well as how the kidney functions, without the need to take any samples of kidney tissue, which is currently how kidney disease is most reliably assessed. MRI is a safe method for imaging the body, as it does not use any radiation.

The MRI techniques for this study have been tested on healthy volunteers prior to recruitment of people with diabetes. This is to ensure the technique is the best it can be and can provide the clearest possible images of the kidneys in the shortest possible time. Some of the imaging techniques that we will use have been provided to us by Siemens specifically for research, and are new techniques for assessing kidneys.

This research has been initiated by the study doctor, Dr Ruth Lim, and is supported by a grant from the Royal Australian and New Zealand College of Radiologists, and Boehringer Ingelheim (manufacturer of the medicine we are studying). The research is also being performed in collaboration with Peter MacCallum Cancer Centre, Melbourne, the University of Utah, New York University and Northwestern University in the United States.

The results of this research will be used by a medical student under the supervision of Dr Ruth Lim to obtain a Doctor of Medicine degree.

3 What does participation in this research involve?

If you are eligible to be part of the study and agree to take part in it, you will first be required to sign the consent form at the end of this document.

You will be participating in a cross-over study, which means that you will receive one medication for 12-14 weeks, then, after a 4-6 week wash out period where you will only take your usual medications, you will then receive the other medication for 12-14 weeks. These medications will be taken **in addition to taking your usual diabetes medications.**

If you are already taking one of the trial medications and you agree to participate in the study, we will ask you to stop taking that medication for a 2-week period, and you will go back to only taking your other routine diabetes medication. This will allow the effects of the drug to clear from your body.

During this 2-week period, a member of the research team will contact you weekly to check that your blood sugar levels remain in an acceptable range. We will do this by asking you to check your blood sugar levels morning and evening. **If you are getting consistently high blood sugar readings of more than 16 mmol/L over 2 days, you need to call the study team to report these results.** The research team will consult the endocrinologist if there are any concerns and contact you with any further instructions. Once the 2-week wash out period is completed, you will be eligible to commence study visit 2.

In a cross-over study the groups each have the different treatments in turn.

The research team will use a computer program to randomly allocate which medication you will start taking.

Study Medication

Empagliflozin is taken orally as a single 10mg tablet once a day for 12-14 weeks.

Sitagliptin is taken as a single 50-100mg tablet orally which will also be taken once a day for 12-14 weeks. The dose you are prescribed by the study doctor will be determined by your kidney function.

These medications will be provided to you free of charge at study visits 2 and 4. The medications will be collected by you from the Austin Hospital pharmacy.

Study Procedures

You will be required to attend the Austin Hospital for 5 visits over a 7-month period for tests including MRI scans, blood and urine tests. These are summarised in the table below with further detail following the table.

Assessment/Procedure	Visit 1 (screening) Week 0	Visit 2 Week 4	Visit 3 Week 16	Visit 4 Week 20	Visit 5 Week 32
Informed Consent	x				
MRI Safety Questionnaire	x		x	x	x
Diabetes Education	x	x		x	
Blood pressure, weight	x	x	x	x	x
Blood tests	x	x	x	x	x
Blood stored		x	x	x	x
Iohexol injection (x-ray dye) and blood test to measure kidney filtration (detailed below)		x	x	x	x
24 hour urine collection		x	x	x	x
MRI with injection of MRI dye		x	x	x	x
Medication Questionnaire		x	x	x	x
Total visit time	1 hour	5 hours	5 hours	5 hours	5 hours

MRI Safety Questionnaire

Study staff will complete the MRI Safety Questionnaire with you. As the MRI machine uses a very strong magnet to take pictures of your kidneys, we need to make sure it is safe for you to have a MRI. You will be asked to fill this in at every visit for your safety. If you answer yes to any of the questions on the MRI Safety questionnaire, we may ask you to sign a consent form authorising Austin Health to obtain your medical records to investigate the MRI safety of any implants that you may have. When you attend the Austin hospital for your MRI scan, a radiographer will review the MRI safety questionnaire with you to ensure it is still safe for you to have the scan.

Before each MRI scan you will need to remove anything made of metal, for example jewellery, hair pins, watches etc. You may also need to remove make up, hair extensions or glitter as these items interfere with MRI pictures. We will ask you to lie on the bed on your back and we will make sure you are as comfortable as possible. You will need to lie very still while the scan is done.

Visit 1: Screening

During the screening visit, the research team need to ensure you are eligible to participate and will need to:

- Review your medical and surgical history and current medications
- Physical assessment of your feet, including checking sensation, pulses, and observing for damage to feet.
- Check your blood pressure & weight
- There will be 10mls (2 teaspoons) of blood taken to check your blood glucose, liver and kidney function and to check if you are anaemic. Anaemia is a condition where there are lower amounts of haemoglobin or red blood cells in your blood than normal.

Red blood cells carry oxygen around the body and anaemia can mean you have less oxygen in your blood. One of the MRI techniques used in the study measures the oxygen levels in the body. It is important that your red blood cell level is within an acceptable range to maintain consistency and to ensure the MRI results are not misinterpreted. If your blood results show that you have moderate or severe anaemia, you will not be able to participate in the study. Blood will also be collected to measure how much natural insulin that your body is producing. The level of insulin that your body naturally produces declines the longer that you have Type 2 diabetes. Measuring this level (C-peptide) will allow us to determine if it is safe for you to take the study drug empagliflozin.

- You will undergo an education session to review monitoring your blood glucose, information about hypoglycaemia (low blood sugar) and management, and an introduction to the two drugs to be used in this study. The research team will be able to answer any questions that you may have.

Visits 2-5: Assessing the effects of the medications

For visits 2-5, you will be required to fast from midnight. A member of the research team will provide you with fasting instructions, including information on checking your blood sugar level and managing your medications.

At **Visit 2**, you will be told which of the two medications, empagliflozin or sitagliptin, you will take first. Before the new medication is started you will be provided with diabetes education from a doctor and/or trained nurse on blood sugar monitoring and the actions of the new medication you are about to take as well as possible side effects. Education will include information about hypoglycaemia as the introduction of a new medication to your treatment may cause you to have low blood sugar levels, although this is unlikely.

The research team will determine which medication you take first by using an online random assignment generator. Each patient taking part in the study will receive one course of each drug.

You will know which medication you are taking, in which order. All patients will have the same tests and same two medications as you.

You will then undergo the following steps during the visit:

1. We will check your weight and blood pressure and visual assessment of your feet.
2. Insertion of an intravenous (IV) cannula into an arm vein, for blood for tests (10mls or 2 teaspoons) to check blood glucose, liver function, kidney function and to check if you are anaemic and for an additional small sample of blood that will be stored to look for other markers of diabetes. Additional blood will be collected (13 ml) to measure different sources of energy that are utilised by the kidneys, to assist our understanding of why Empagliflozin has been shown to slow the progression of kidney disease. This cannula will also be used to inject MRI dye during the MRI examination.
3. 24-hour urine collection: we will provide you with a container to collect urine for 24 hours and ask you to bring this in to your visit. We will contact you the day prior to your study visit to remind you to start the 24 hour urine collection.

4. MRI examination: The MRI will take up to 60 minutes to complete and will include imaging to look at the structure and function of your kidneys. You may be asked to hold your breath during certain parts of the scan. Just before the scan, we will give you 250 mls of water to drink.
5. Iohexol injection (x-ray dye) and blood samples to check kidney filtration. Iohexol is a dye commonly used in CAT scans to highlight tissues in the body. It can also be used to check how well the kidneys filter substances, which is how it will be used in this study. It will be compared to the results of your MRI scan. It involves injection of a small amount (5mls or 1 teaspoon) of iohexol. We are only using a very small amount – usually a much larger amount (approximately 100ml) is given for CAT scans). It will involve insertion of a second IV cannula. This is so that the blood samples are not contaminated by the dye. We will give you another 250 mls of water to drink before we take the first blood sample.

   There will be 5 blood samples of 5mls (total of 25mls or 5 teaspoons) taken over approximately 4 hours. One sample will be taken prior to you receiving the iohexol injection and then 90mins, 120mins, 180mins & 240mins after the iohexol injection.
6. You will be asked to complete a questionnaire about your experience with your current medications. This questionnaire should take you approximately 5 minutes to complete.

After Visit 2, you will be asked to take the first medication you are given for a total of 12-14 weeks.

When you start taking either Empagliflozin or Sitagliptin, a member of the research team will call you weekly for 4 weeks, and then every 4 weeks after that, to check how you are managing with the new medication. This will give you an opportunity to discuss any potential side effects of the drugs, or concerns with your blood sugar level, and you can also contact the research team at any time during the study if you have any concerns regarding the medication or your blood sugar levels. You will also be provided with a medical emergency card containing instructions on who to contact after-hours in the event of an emergency. You will be asked to keep all the medication packaging and bring it back at your next visit.

You will then return for **Visit 3**, where you will undergo exactly the same steps as for Visit 2. After Visit 3, you will stop taking the first medication, and have a 4-week period where you will go back to only taking your usual diabetes medication. This will allow the effects of the first drug to clear from your body.

A member of the research team will call you weekly after you have stopped taking the additional drug, to check that your blood sugar levels stay within an acceptable range.

After the 4-6 week break, you will return for **Visit 4**, where you will undergo the same steps as for Visits 2 and 3, to get baseline information before you start the other medication.

Next, you will receive another 12-14week course of treatment with the second medication. A member of the research team will call you weekly for 4 weeks, and then every 4 weeks after that, to check how you are managing with the new medication. This will give you an opportunity to discuss any potential side effects of the drugs, or concerns with your blood sugar level.

The final visit, **Visit 5**, will occur after this, to examine the effects of the second drug, undergoing exactly the same steps as for Visits 2, 3 and 4. . We will again ask you to bring the empty packets of the second medication with you for this visit, to help us keep a record of the medication that you have taken.

Once you have completed all 5 visits, you will have completed the research study. A member of the research team will call you 1 week after you have completed the study to ensure your blood sugar levels are within an acceptable range. The research team will arrange for you to attend the diabetes clinic within 4 weeks of completing the study, so the endocrinologist can review your medications and blood sugar levels.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

Costs:

There are no additional costs associated with participating in this research project. All medication, tests, and medical care required as part of the research project will be provided to you free of charge.

You will be provided with a car parking voucher to cover your parking fees on all study visits. Additionally on visits 2-5, you will be provided with a $50 reimbursement fee for each visit to cover your travel expenses and to compensate you for your time. You will be required to fast for study visits 2-5, until all tests are completed. Once you have completed fasting, we will provide you with a snack prior to sending you home.

4 What do I have to do?

If you decide to be in this study, there are certain things you must do before, during, and after the study period. Some of these are listed below:

- It is important that you take the medication as prescribed around the same time each day and follow all the instructions provided by research staff.
- Please let the research team know if there is any reason that you cannot participate in the study.
- You are able to take all of your usual medications.
- There are no restrictions to your lifestyle or diet if you choose to participate in this study, other than fasting prior to study visits 2-5. We request that you do not donate blood during the study period because it could affect the results of the study.
- It is important that you tell the research staff all of the information you know about your health and all medications that you may be taking throughout the study period. If there are any changes to your current medications please advise the research staff, as this may affect the results of the study.
- It is also important to tell research staff about any changes in your health, whether or not you think they are related to the Study Drugs or not.
- You need to inform the research staff if you have been involved in any other clinical studies or have been involved in any other studies within 30 days prior to this study, as it may impact whether or not you can take part in this study.
- You cannot be involved in any other studies involving investigational drugs while you are participating in this study.
- It is important that you follow the research team's instructions throughout the study. If you have questions or want further information, contact the study doctor or research staff.

- Only the study participants should take the study drugs. All drugs must be kept out of the reach of others, especially children.

5 Other relevant information about the research project

It is planned that altogether about 36 patients with Type 2 diabetes will take part in this study. All patients who participate in the study will undergo the same process as you, including taking the additional medications, the blood and urine tests, and MRI examinations. This is a new study that is being performed at Austin Health.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Austin Health.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. There will be no change to your treatment or care if you decide not to take part in this project.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research. It is hoped that in future, the results of the study will provide patients with diabetes with a safe and accurate way to monitor diabetic kidney disease.

9 What are the possible risks and disadvantages of taking part?

If there are any unexpected findings as a result of the MRI that will affect your medical care, these will be discussed with your treating doctor.

Medical treatments may cause side-effects. You may have none, some or all of the effects listed. They may be mild, moderate or severe. You should tell your doctor if you experience any side-effects, and the research team will have regular phone contact with you, where any side-effects will be discussed.

Medications

Boehringer Ingelheim (manufacturer of Empagliflozin) has completed 15 clinical drug trials for Empagliflozin. Merck and Co (manufacturer of Sitagliptin) has completed 25 clinical drug trials for Sitagliptin. The reported side-effects from these studies are outlined in the following tables:

Place Patient Label Here

Reported side-effects of Sitagliptin:

Common (<10%)	Uncommon (<1%)	Rare (<0.1%)

• Back pain
• Headache
• Upper respiratory tract infections
  • inflammation of nasal passages and throat
	• constipation
	• pancreatitis (inflammation of the pancreas) which causes persistent, severe abdominal pain
	• Dizziness
		• Severe allergic reaction
		• Disabling joint pain
		• Symptoms of allergic reaction include:
		  o Itching
		  o Difficulty breathing
		  o Swelling in the mouth, lips, face
		  o Skin condition- shedding skin

Reported side-effects of Empagliflozin:

Common (<10%)	Uncommon (<1%)	Rare (<0.1%)

• Genital infections, reported more frequently in women
• Increased urine production
• Urinary tract infection
• Itching
• Thirst
• Allergic skin reaction, eg skin rash
	• Dehydration
	• Low blood pressure
	• Painful urination
		• Ketoacidosis- build-up of dangerous chemical substances in the blood, called ketones, when the body breaks down fat for energy.
		  – Symptoms include: nausea, vomiting, rapid breathing, abdominal pain.
		  – If you experience any of these symptoms, you must seek medical attention.
		• Serious allergic reaction
		Symptoms of allergic reaction include:
		  – Itching
		  – Difficulty breathing
		  – Swelling in the mouth, lips, face
		• Serious bacterial infection that destroys the tissue under the skin in the area between your anus and genitals
		Symptoms include:
		  – Pain or tenderness
		  – Swelling
		  – Redness of the skin
		  – Fever
		  – weakness

The research/diabetes doctor will review your current medications to ensure it is safe for you to take the additional drugs, and that there is no possibility of the additional drugs interacting with these medications.

The research team will maintain regular telephone contact with you during the study. You are encouraged to inform the research team of any side-effects that you may experience during the course of the study. You will be given a participant emergency card at Visit 1, providing information on who to contact in the unlikely event of an emergency. Any side-effects will be documented in your study file, medical record and if necessary a follow-up appointment with the Endocrinology team will be organised to ensure you are followed up appropriately.

Education will be provided to you by a doctor or nurse about the possible side effects of each study drug before you start any new medications, steps to take to avoid serious side effects such as ketoacidosis, and management of side effects.

Insertion of Intravenous cannula and collection of blood samples

There are no major risks associated with having an intravenous cannula inserted and blood collected. It is possible you may feel some discomfort during the cannula insertion. You may feel a sting when the needle is put in your arm. It is possible there may be some bruising, swelling or bleeding where the needle enters the skin, and risk of minor infection. Some people can feel a little light-headed when a needle is inserted.

MRI

MRI stands for magnetic resonance imaging. A MRI scanner is a machine that uses electromagnetic radiation (radio waves) in a strong magnetic field to take clear pictures of the inside of the body. Electromagnetic radiation is not the same as ionising radiation used, for example, in X-rays. The pictures taken by the machine are called MRI scans.

We will ask you to lie on a table inside the MRI scanner. The scanner will record information about your kidneys. It is very important that you keep very still during the scanning. When you lie on the table, we will make sure you are in a comfortable position so that you can keep still.

The scanner is very noisy and we will give you some earphones to reduce the noise. Some people may experience symptoms of claustrophobia from lying in a confined space. If you do experience discomfort at any time during the scan, you will be able to alert staff by pressing on a call button provided to you.

There are no proven long-term risks related to MRI scans as used in this research project. MRI is considered to be safe when performed at a centre with appropriate procedures. However, the magnetic attraction for some metal objects can pose a safety risk, so it is important that metal objects are not taken into the scanner room.

We will thoroughly examine you to make sure there is no reason for you not to have the scan. You must tell us if you have metal implanted in your body, such as a pacemaker or metal pins.

The MRI scans we are taking are for research purposes. They are not meant to be used to help diagnose, treat or manage a particular condition. A specialist will look at your MRI scans for features relevant to the research project. On rare occasions, the specialist may find an unusual feature that could have a significant risk to your health. If this happens, we will contact you or your treating doctor to talk about the findings. We cannot guarantee that we will find any/all unusual features.

MRI dye

The MRI dye is approved by the TGA and is used routinely and repeatedly in patients to help with assessment of diseases such as cancer and infections. It is removed from the body by the kidneys, and therefore it is only given when the kidneys are filtering urine adequately. Patients with very severe kidney disease should not receive MRI dye, as there is a risk of it causing a rare condition called Nephrogenic Systemic Fibrosis that causes thickening and hardening of the skin and soft tissues. At each study visit, we will check your kidney function from a blood test taken when we insert the intravenous cannula, prior to you having the MRI scan and MRI dye. Although you may have reduced kidney function, as per standard clinical care, it is safe for you to have the MRI dye. If there is any deterioration in your kidney function during the study and it is no longer safe for you to have the MRI dye, we will notify you and withdraw you from the study.

The most common reported side effects are a warm feeling, and pain at the injection site. There is also a low risk of side effects such as nausea, or being allergic to the dye. Allergy to the dye is uncommon, occurring in <1% of patients and symptoms usually appear within an hour of having the dye. An allergic reaction usually affects the skin with rash, itching or redness, and very rarely can cause difficulty breathing.

It has recently been shown that certain formulations of MRI dye are more likely to stay within the body rather than being removed by the kidneys, including in the brain. The MRI dye that you will receive (Dotarem) is considered the safest MRI dye because of its chemical structure, and in animal tests has not been found to stay within the brain, nor has it been found to stay within the brain in humans to date. You will receive a standard dose to allow us to assess how the kidneys filter urine and the blood vessels supplying the kidneys.

Iohexol

You will also receive a very small dose of another dye called iohexol to see how your kidneys process the dye. Iohexol (Omnipaque 300) is a dye made from iodine that is routinely used for CAT scans and is part of standard clinical practice. The amount that you will receive is 5 mls, about 1 teaspoon, where the usual dose given for a CAT scan is between 70-150 mls. In patients with very severe kidney disease, this can cause damage to the kidneys in large doses. However, if you are eligible for this study, you have normal kidney function or mild kidney disease, and are not at risk of this. We will check your kidney function at the beginning of each study visit, to ensure it is safe for you to receive the dye. If you are on metformin, there is also a very rare risk of developing a condition called lactic acidosis after receiving iodine-based dye. However, this can only occur if the kidneys are damaged by the dye, which can only happen with severe kidney disease, and so you are not at risk of this.

If there is any deterioration in your kidney function, which we will check with blood tests during the study, and it is no longer safe for you to have the dye, we will notify you and withdraw you from the study. The most common reported side effect of iohexol is a warm feeling when the dye is injected. Nausea is an uncommon side effect. Allergy to iohexol is rare, occurring in less than 1% of patients. Symptoms of allergy to iohexol are rash, redness, difficulty breathing, and itching. As part of standard clinical practice, we will ask you if you have any allergies prior to giving you any dye and will provide treatment should an allergic reaction develop.

10 What will happen to my test samples?

All participants will undergo kidney MRI, blood tests and 24hr urine samples during the study, which will be compared to each other. Blood and urine samples will be sent immediately to Austin

Pathology for routine testing**.** Blood and urine samples will be destroyed after 7-10 days when routine testing has been completed. MRI images will be analysed by the study team.

A sample of blood will also be stored for future analysis of markers in the blood that may help with identification and monitoring of complications of diabetes, and by signing the consent form, you agree to the storage of your blood sample.

This sample of blood will be stored in a freezer at the Heidelberg Repatriation Hospital in a locked room for an indefinite time. If the frozen sample deteriorates over time, it will be destroyed according to Austin health guidelines. The sample will only be used for other ethically approved research projects.

All study test results, imaging and data will be made anonymous for all analysis and any subsequent publications or presentations, so they cannot be identifiable as belonging to you.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you will be able to take all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments, since they might interfere with each other.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the study team up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- The imaging test being shown not to be effective

- The imaging test being shown to work and not need further testing

15 What happens when the research project ends?

There is no follow-up after you have completed the imaging and surveys for this study. A member of the research team will call you 1 week after you have completed the final study visit, to check that your blood sugar levels are within an acceptable range. An appointment will be made for you at the diabetes clinic within 4 weeks of completing the study, in order to have an endocrinologist review your medications and blood sugar levels. Once the results of the study are analysed, it is planned that they will be presented and published for other doctors who specialise in imaging tests.

It is anticipated that this study will help provide evidence that empagliflozin protects the kidneys in patients with Type 2 diabetes. The findings of this study will also assist us in planning a larger study in future.

16 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Information obtained during the course of this project will be anonymised during analysis so that it cannot be identified as belonging to you. A record that allows the research study doctor to re-identify you if required will be kept in a secure locked office in the Radiology Department of Austin Health.

Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law. Information will be stored by the research team as required by law for a period of 15 years following the study, and then will be destroyed.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities of the institution relevant to this Participant Information Sheet, Austin Health, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel, authorised representatives of the Sponsor as well as regulatory authorities as noted above. Anonymised information that cannot be identified as information belonging to you may be shared with Peter MacCallum Cancer Centre, the University of Utah, New York University, Northwestern University and Siemens Healthineers to assist with image interpretation.

It is anticipated that the results of this research project will be published and/or presented to other medical professionals. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. All information will be anonymised for analysis and any subsequent presentation/ publication.

In accordance with relevant Australian and Victorian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also

have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

18 Who is organising and funding the research?

This research project is being conducted by Dr Ruth Lim and funded by the Royal Australian and New Zealand College of Radiologists, Boehringer Ingelheim, and the Radiology and Endocrinology Departments at Austin Health.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Austin Health. This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor Dr Ruth Lim on 9496 5000 (business and after hours) or:

Clinical contact people are: (business hours)

Name	Julie Smith
Position	Radiology Research Co-ordinator
Telephone	(03) 9496 6794
Email	radiologyresearch@austin.org.au

Place Patient Label Here

Name	Lucy Milligan
Position	Radiology Research Nurse
Telephone	(03) 9496 6794
Email	radiologyresearch@austin.org.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Position	Manager, Ethics and Governance
Telephone	(03) 9496 3248
Email	ethics@austin.org.au

Place Patient Label Here

Consent Form - *Adult providing own consent*

Title	Using MRI to assess impact of add-on empagliflozin on renal physiology in Type 2 diabetic patients
Short Title	Role of MRI in evaluating the impact of empagliflozin in patients with Type 2 diabetes.
Project Sponsor	RANZCR, Boehringer Ingelheim, Radiology and Endocrinology Departments, Austin Health
Principal Investigator	Ruth Lim
Location	Austin Health

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Austin Health concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please _____

Signature _____ Date _____

Declaration by Study Doctor/Senior Researcher[†]

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher[†] (please print) _____

Signature _____ Date _____

[†] A senior member of the research team must provide the explanation of, and information concerning, the research project.
Note: All parties signing the consent section must date their own signature.