Use of Juvenile IGF-1 in Breeding Programs

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Background

Insulin-like Growth Factor-1 (IGF-1) is a naturally occurring peptide with roles in both the endocrine (hormonal) systems, along with autocrine/paracrine activity at a cellular level. IGF-1 can be measured relatively easily in blood with appropriate techniques. The concentration of IGF-1 circulating in the blood plasma of weaned (juvenile) piglets has significant genetic correlations with several economically important performance traits (Luxford et al., 1998; Hermesch, 2000; Hermesch et al., 2001; Lahti et al., 2001).

Information from IGF-1 concentration can be used as an early physiological indicator of traits traditionally measured later in life. Performance traits include average daily gain (ADG), backfat (BF) and feed conversion ratio (FCR). Specifically, moderate to high genetic correlations between IGF-1 levels and FCR point towards its use as a lower cost indirect alternative to measuring FCR directly. IGF-1 provides correlated information on this performance trait, which many small scale breeding operations are not in a position to otherwise measure directly and/or on a high proportion of animals. Moreover, genetic correlations between IGF-1 and other traits provide additional information towards the overall breeding objective. Further, information on an animal's potential performance is obtained at an early age, and could be used for decision making purposes. For example, which animals to performance test if testing capacity is limited, or early castration decisions are required.

The test for juvenile IGF-1 is now patented as the PrimeGRO® LSM, and is available commercially in Australia. The objective of this paper is to provide a summary of trial results to date, with additional research results from other studies, and to demonstrate how Australian pig breeders could use information from juvenile IGF-1 in their breeding program.

Summary of Trial Results

Original studies (reported by Bunter, 1996) on the relationships between IGF-1 and performance traits were conducted by Bunge Meat Industries (BMI) in populations developed from predominantly Landrace and Large White origins. The age at testing for IGF-1 concentration was considerably younger than that routinely investigated in other scientific studies. Historically, the association between IGF-1 and growth related traits was commonly studied in growers or finishers due to an association between IGF-1 and growth hormone (GH) levels at these ages. Juvenile measures combined with closed population issues generated scepticism from some pig breeders and scientists as to applicability of results obtained to other breeding herds. This, in turn, motivated further analyses of different lines within BMI which included infusions from other breeds,

following extensive testing for juvenile IGF-1 (see Hermesch, 2000), and the conception of small trials in other populations. Increasing the genetic diversity of populations studied and/or the management systems under which animals are performance tested provides more robust evidence for results observed in the original study. A summary of results from the different studies is presented in Table 1. The similarity (in terms of direction and magnitude) of parameter estimates across diverse pig populations suggests that earlier conclusions (based on results from the BMI 1 study) are unlikely to be specific to the BMI populations of pigs, although the value of estimated correlations may vary between studies.

The conclusions that can be drawn from results to date are that IGF-1 is a moderately heritable measure, and downward selection should result in favourable correlated responses in BF and FCR. The pooled heritability estimate for juvenile IGF-1 is 0.24 ± 0.06 based on data presented in Table 1. Pooled estimates of genetic correlations between IGF-1 and BF or FCR are 0.48 ± 0.07 and 0.52 ± 0.18. Moreover, results for these traits generally remain consistent where performance test traits are evaluated over either short or long test periods (BMI 1 versus USA 1 & 2, UK 1 & 2), under *ad-lib* or restricted feeding regimes (BMI 1 & 3 versus BMI 2), and for early-weaned pigs (USA 1 & 2 studies versus rest). Moreover, the general relationship between IGF-1 measures and fat appear to be consistent across species. For example, positive genetic correlations between IGF-1 and fat measures are also observed in the study of Johnson et al. (2001) in Angus cattle.

Table 7. A summary of heritability estimates for IGF-1, along with genetic correlations between IGF-1 and backfat or feed conversion ratio, where available (NE: not estimated), from various studies.

Study	Heritability	Genetic correlations between IGF-1 &	
		BF	FCR
BMI 1 (1996)	0.20	0.29	0.84
BMI 2 (2000)	0.23	0.46	0.51
BMI 3 (2001)	0.24	0.46	NE
USA 1 (2001)	0.58	0.54	0.59
USA 2 (2001)	0.44	0.49	0.50
UK 1 (2001)	0.53	0.81	NE
UK 2 (2001)	0.42	0.68	NE

BMI 1: Lines 1 & 2 (LW and LR based) – individually penned boars, short test, *ad-lib* feeding.

BMI 2: Lines 5, 7 & 8 (synthetics of LW, LR and Duroc breeds) – group test with electronic feeders, restricted feeding.

BMI 3: Lines 1, 2 and 7 (as above) – group pen test, *ad-lib* feeding.

USA 1: Bell Farms LW - group test with electronic feeders, *ad-lib* feeding.

USA 2: Bell Farms LR - group test with electronic feeders, *ad-lib* feeding.

The consistency of results from studies providing parameter estimates for various populations is also supported by evidence accumulating for a positive relationship between IGF-1 and fat deposition in various physiological studies. Stimulation of cultured porcine preadipocytes with physiological concentrations of IGF-1 has been demonstrated to increase the number and size of fat cell clusters (Chen et al., 1995) and

their ability to accumulate lipids (Boone et al., 2000). In live pigs, coadministration of IGF-1 with porcine growth hormone reduces the ability of GH to increase gain while suppressing backfat (Klindt et al., 1998). Thus, high levels of IGF-1 have demonstrated negative consequences in terms of fat accretion.

Less direct evidence for the association between IGF-1 and efficient lean meat growth is discussed in the paper by Hermesch et al. (2001) (also see workshop notes, 2001). Similar patterns of genetic correlations were evident between piglet traits at birth and juvenile IGF-1 or BF (end of test). Estimates of genetic correlations between juvenile IGF-1 or BF and piglet weight at birth were both negative (-0.33±0.19 and –0.43±0.17), indicating that genetically leaner pigs have heavier weights at birth and lower levels of IGF-1 in the young pig. Herpin et al. (1993) had previously suggested that selection for lean tissue growth appeared to have effects on body and tissue composition, metabolic and hormonal state, and fat metabolism, leading to heavier pigs at birth.

Use of IGF-1 to Improve Response to Selection

Improvements in response to selection through use of information on additional traits, such as IGF-1, can be evaluated using Index calculations. Genetic parameters and economic values fairly typical of the traits usually included in the breeding objective of **terminal** sire lines are presentedin Table 8. Pooled parameter estimates for IGF-1 noted above are also used. The standard deviation of this breeding objective is $6.37.

Table 8. Phenotypic standard deviations (σ_p), economic weights (v: per slaughter pig), heritabilities (h^2), litter effects (c^2) along with correlations assumed for index calculations.

Trait	σ_p	v	h^2	c^2	Correlations[1]			
					IGF-1	ADG	BF	FCR
IGF-1	44	0	0.24	0.05		0.10	0.20	0.10
ADG	65	0.07	0.30	0.10	0		0.20	-0.10
BF	2.1	-2.5	0.40	0	0.48	0.10		0.15
FCR	0.3	-28	0.20	0	0.52	-0.25	0.25	

[1]Phenotypic correlations above the diagonal; genetic correlations below

Abbreviations:

IGF-1 Insulin-like growth factor-I (nannograms/millilitre)
ADG Lifetime growth rate (grams/day)
BF Backfat at the P2 site (millimetres)
FCR Feed Conversion Ratio (kilogram feed/kilogram gain)

Assume that at selection, candidates have on average information from their parents, 4 full sibs and 20 half sibs recorded for ADG and BF. If IGF-1 were measured, the same amount of information is assumed recorded, although potentially more could be available. However, feed conversion data, if recorded, is likely to be limited to relatively few animals. For example, many selection candidates may not have their own records, and will rely on records from relatives (their sire, full-sib or half-sibs) to provide information. If the top five percent of boars (selection intensity i = 2.063) and 20% of gilts (i = 1.400) are selected as parents, an average selection intensity of i = 1.7315 is achieved. The

response to selection in individual traits after one round of selection, for the given selection intensity, along with financial change in the overall breeding objective can then be evaluated for selection indices using differing amounts of information (Table 9).

Under the defined breeding objective and selection intensities, performance recording for ADG and BF alone (Index 1) results in a response of $6.82 per slaughter pig in one generation of selection. For comparison, using additional information on IGF-1 (Index 2) increases response by 7%, whereas only slightly better would be achieved if selection candidates were instead tested directly for FCR (Index 3: 8% improvement) but significant information from relatives was not available. For many breeders, selection candidates are not routinely tested for FCR and/or information from relatives is limited or not available. For example, if data on FCR is restricted for many selection candidates to information provided from few relatives, improvements in response from measuring FCR directly are relatively small (0 or 2% for Indices 4 & 5). Increasing records on FCR to own, sire, 1 FS and 4HS increases index accuracy to 0.686 (11% improvement) whereas this lowers to 4% if candidates do not have their own record, but do have some relatives with records. Reality probably lies somewhere around this 4-11% region.

Table 9. Traits included in the selection index along with response to selection for individual traits (assuming i = 1.7315), response in the overall breeding objective (R_H) after one generation, and Index accuracy (R_{IH}).

Trait	Index 1	Index 2	Index 3	Index 4	Index 5
IGF-1	-	✓	-	-	-
ADG	✓	✓	✓	✓	✓
BF	✓	✓	✓	✓	✓
FCR	-	-	own	FS or sire	HS
Response in individual traits (genetic)					
ADG	23.9	23.2	23.0	23.6	23.8
BF	-1.35	-1.33	-1.25	-1.33	-1.35
FCR	-0.062	-0.083	-0.094	-0.071	-0.064
Response in the breeding objective (R_H)					
Absolute response ($)	6.82	7.27	7.39	6.94	6.86
Relative response	100	107	108	102	100
Accuracy of Index (R_{IH})	0.618	0.659	0.669	0.630	0.621

Own: own record; sire: record on sire only; FS: record on 1 full-sib only; HS: record on 1 half-sib only. Indices 4 and 5 represent accuracy of selection for candidates without own records.

For trait abbreviations see Table 1.

In the situation of no or limited testing for an economically important trait such as FCR, wider testing for a trait highly correlated with FCR may yield a better response. Thus, routine testing for an indirect measure (such as in Index 2) replaces a lack of information for the direct measure of interest (FCR). Strategies examined in the following section are for the scenario where FCR is not recorded, and complete testing of all animals for IGF-1 is not a feasible option.

Strategies for Testing Juvenile IGF-1

For any trait included in the breeding objective the maximum response will always be achieved by testing all selection candidates. The same principle operates for indirect

measures and/or selection criteria. However, this goal is usually balanced with other constraints (eg. cost of testing, facilities and labour available etc.) and generally requires a trade off between what response could be achieved in theory, and what is practicable from an operational and cost viewpoint. Assuming that resources for performance testing are limited, it can be useful to examine what level of testing is required to achieve accurate EBVs for IGF-1. Changes in accuracy for this trait can be directly related to improvements in the overall breeding objective if it is assumed that no concurrent changes to the testing procedures for other traits are made when testing for IGF-1 is introduced. The exact accuracy's of EBVs were calculated for this purpose by directly inverting the left hand side of the mixed model equations for estimating breeding values, while varying the number of sires, dams (litters) and tests available. Heritability of IGF-1 and common litter effects assumed were 0.25 and 0.05 respectively.

The accuracy of EBVs is only presented (Table 10) for examples where the balanced design for testing does not exceed the total number of tests available, or use less than 90% of the number of tests targeted (non-valid options are marked with an 'X'). Generally, increasing the total number of animals tested for IGF-1 increases the accuracy of evaluation as expected. It also increases the number of options for testing strategies, particularly as the number of sires with progeny increases. Moreover, testing larger groups of animals together will provide more effective information if other effects (eg. assay batch) must be included in the models for predicting breeding values.

Table 10. Accuracy of EBVs for IGF-1 for selection candidates when the number of sires and tests differ, and when testing is balanced across sires and litters.

No.	No.	Number of progeny tested per litter									
Sires	Tests	1	2	3	4	5	6	7	8	9	10
1	10	**.37**	.36	.35	.34	.34	X	X	X	.26	.26
	20	**.38**	**.38**	**.38**	**.38**	**.38**	.37	X	X	.35	.35
	30	.38	**.39**	**.39**	**.39**	**.39**	**.39**	**.39**	X	.38	.38
	40	.38	.39	.39	**.40**	**.40**	**.40**	**.40**	**.40**	.39	.39
	50	.38	.39	.39	**.40**	**.40**	**.40**	**.40**	**.40**	**.40**	**.40**
	100	.39	.39	.40	.40	**.41**	**.41**	**.41**	**.41**	**.41**	**.41**
2	10	**.45**	.44	X	X	.44	X	X	X	X	X
	20	.47	.47	.47	**X**	**.48**	X	X	X	.46	.46
	30	.48	.48	**.49**	**X**	**.49**	**X**	**.49**	X	X	X
	40	.49	.49	.49	**.50**	**.50**	**.50**	**X**	**X**	**.50**	**.50**
	50	.49	.50	.50	.50	**.51**	**.51**	**X**	**.51**	.50	.50
	100	.51	.51	.52	.52	.52	.52	**.53**	**.53**	**.53**	**.53**
5	10	.47	**.48**	X	X	X	X	X	X	X	X
	20	.49	.50	.50	**.51**	X	X	X	X	X	X
	30	.50	.51	.52	**X**	**X**	**.53**	X	X	X	X
	40	.51	.52	.52	.53	**X**	**X**	**X**	**.54**	X	X
	50	.52	.53	.53	.53	.54	**X**	**X**	**X**	**.55**	**.55**
	100	.54	.55	.55	.56	.56	.56	**.57**	**.57**	**.57**	**.57**
10	10	**.47**	X	X	X	X	X	X	X	X	X
	20	.49	**.50**	X	X	X	X	X	X	X	X
	30	.50	.50	**.52**	X	X	X	X	X	X	X
	40	.51	.52	.52	**.54**	X	X	X	X	X	X
	50	.51	.52	.53	.54	**.55**	X	X	X	X	X
	100	.54	.55	.55	.55	.56	X	X	X	.57	**.58**

X: option would exceed fixed number of tests, OR less than 90% of tests would be used

However, the effect of increasing the number tested per litter depends on the total number of tests available, and the number of sires represented by progeny in a single test group. Generally, when the number of tests is low (eg. 10) fewer progeny per litter should be tested in order to **increase the number of litters tested per sire**. For example, when the number of tests is restricted to only 10 or 20, the accuracy of EBVs for selection candidates is lower when 1 or 2 litters (10 progeny/litter) are tested compared to testing 1 progeny each from 10 to 20 different litters. However, as the number of tests is increased, increasing the number of progeny tested per litter will increase accuracy of EBVs for selection candidates. Moreover, it will reduce the number of candidates available for selection who do NOT have records for IGF-1 (and whom would subsequently have a lower accuracy EBV).

Table 11. Accuracy of sire and dam EBVs for IGF-1 with a different number of progeny tested per litter (number tests=100, corresponding number of litters/sire in brackets, testing balanced across sires and litters).

No. Sires		Number of progeny tested per litter									
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	Sire	.0	.0	.0	.0	.0	.0	.0	.0	.0	.0
	Dam	.26	.34	.40	.43	.46	.48	.50	.52	.53	**.54**
	litters)	(100)	(50)	(33)	(25)	(20)	(16)	(14)	(12)	(11)	(10)
2	Sire	**.62**	.61	.60	.59	.59	.58	.57	.56	.55	.55
	Dam	.26	.34	.39	.43	.45	.47	.49	.50	.51	**.52**
	litters)	(50)	(25)	(16)	(12)	(10)	(8)	(7)	(6)	(5)	(5)
5	Sire	**.68**	.66	.63	.63	.62	.59	.59	.59	.55	.56
	Dam	.25	.33	.38	.42	.44	.45	.47	.47	.48	**.49**
	litters)	(20)	(10)	(6)	(5)	(4)	(3)	(3)	(2)	(2)	(2)
10	Sire	**.60**	.58	.54	X	.53	X	X	X	.47	.47
	Dam	.25	.33	.37		.43				.46	**.47**
	litters)	(10)	(5)	(3)		(2)				(1)	(1)

No. progeny tested per sire: 100 (1 sire); 50 (2 sires); 20 (5 sires); 10 (10 sires)

Examination of the accuracy of sire and dam EBVs (who do not have records) is also informative (Table 11). Within any given number of sires (other than for 1 sire whose progeny are tested alone), the accuracy of sire EBVs is highest where the number of litters tested per sire is maximised. The reverse trend occurs for dam EBVs: increasing the number tested per litter is more informative. Consequently, the number of progeny tested per sire and dam, along with the number of sires and dams represented, both influence the average accuracy of EBVs for their progeny, the selection candidates. For a fixed number of tests and litters per sire (N=100, litters=10), it can be observed that the highest accuracy's of a sire's EBV (0.66) occurred for 5 sires/management group with two progeny tested/litter, giving 20 progeny tested in total per sire. Reducing the total number of progeny tested per sire to 10 reduced accuracy to 0.60. On the other hand, increasing the total number of progeny tested per sire to 50 had no benefit (accuracy=0.59) because progeny from fewer sires were compared in the same group (and the value of comparing sibs with each other is less).

Results presented above suggest a few guidelines for achieving accurate information from IGF-1 testing. These can be summarised as:

- Including progeny from more than 1 sire in a test group substantially increases accuracy of EBVs for selection candidates. The increase from one to two sires is significantly larger than the increase from two to five. DO NOT create IGF-1 test groups containing progeny from one sire only.
- The number of sires producing progeny per week will generally determine the optimum number of pigs to test per litter for a fixed number of tests/week. Where progeny from two to five sires are tested concurrently, testing up to 4 pigs per litter would appear adequate. Testing fewer pigs per litter will decrease overall accuracy (of candidates both with and without records for IGF-1), whereas testing more does not substantially increase the accuracy of EBVs for animals with records, but does reduce the number of selection candidates without records. Accuracy of EBVs for selection candidates with no records for IGF-1 will be lower, but this difference will reduce in importance as other data accumulates.
- More extensive testing may be used initially to increase the accuracy of parental, and thus progeny, EBVs quickly. For example, the accuracy of sire EBVs does not exceed 0.5 until approximately 40 tests (for 2-5 sires) are achieved. More tests would be required for more sires, and if tests are spread over several testing dates (as is common). Breeders should aim at a level of testing which allows them to test at least 20 progeny per sire, and/or progeny from at least 5 litters per sire. There is probably little advantage to testing excessively large numbers of progeny per sire, unless they provide significant information for dam merit (ie the dam has not had progeny tested previously). Continuing testing at a lower level is feasible when genetic evaluation is via PIGBLUP, as all historical data is used.
- Increasing the number of tests is of relatively more benefit when progeny from several sires are available for testing. A large number of tests for a relatively small population would be counter-intuitive.

Other Issues

Prior to implementing testing for IGF-1 there are other factors that should be considered. These relate generally to the number of tests which breeders can invest in, along with the breeding objective of the population(s) of interest.

When relatively few tests are feasible, it becomes much more important to test animals effectively. This can be considered not only with respect to how many pigs to test per litter and sire, but also in how to construct test groups for a weekly fixed number of tests. For example, if only a small number of tests can be conducted on a weekly basis, it could be possible to test twice as many animals once per fortnight (for example) providing weaning is sufficiently early that animals could be bled after weaning and before 35 days of age. This would maximise test group size, and age differences at testing would be automatically accounted for in the analyses. However, it may be necessary to then define management groups such that pigs weaned in the first week of a fortnight are allocated to group 1, and pigs weaned in the second week are allocated to group 2 (via user defined management groups).

With respect to breeding objective(s), the breeding goal can also be used to determine which population attention should be focussed on to performance test for new traits such

as IGF-1. For example, if FCR is not an important component of the breeding objective (eg. growth and efficiency related traits are generally only half as important in maternal lines), testing for IGF-1 may be allocated to other lines where efficiency is more important (eg terminal sire lines). If only relatively few tests can be achieved, it may take some time before sufficient data is accumulated for benefits to be realised. Thus, it may be advantageous to concentrate attention into fewer breeds or lines, thereby accumulating useful data, and the benefits, faster.

Moreover, if only a few pigs per litter are to be tested for IGF-1, it may also be desirable to consider whether testing should be conducted in both sexes. For example, wider testing of males will increase their accuracy of selection, thereby improving response. This is the usual strategy for allocating animals to more expensive performance test procedures. On the other hand, testing some females is also desirable given that a higher proportion of females than males ultimately become parents, and thus also contribute to progeny information. If females remain in the nucleus herd for some time, they will accumulate significant amounts of information from their progeny data, providing improved accuracy of EBVs for progeny without their own IGF-1 records. This will be less likely if the turnover of sows is high. Alternatively, the value of testing females could also be improved if females are ultimately culled, where possible, using EBVs. That is, selection pressure is increased on the female side post selection.

Summary

IGF-1 does provide useful information towards the breeding objective of populations focussed on efficient lean meat growth. However, with a limited investment in testing procedures, care must be taken to ensure that the data collected is informative and effectively used. Some general guidelines for breeders towards this aim are presented in this document.

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